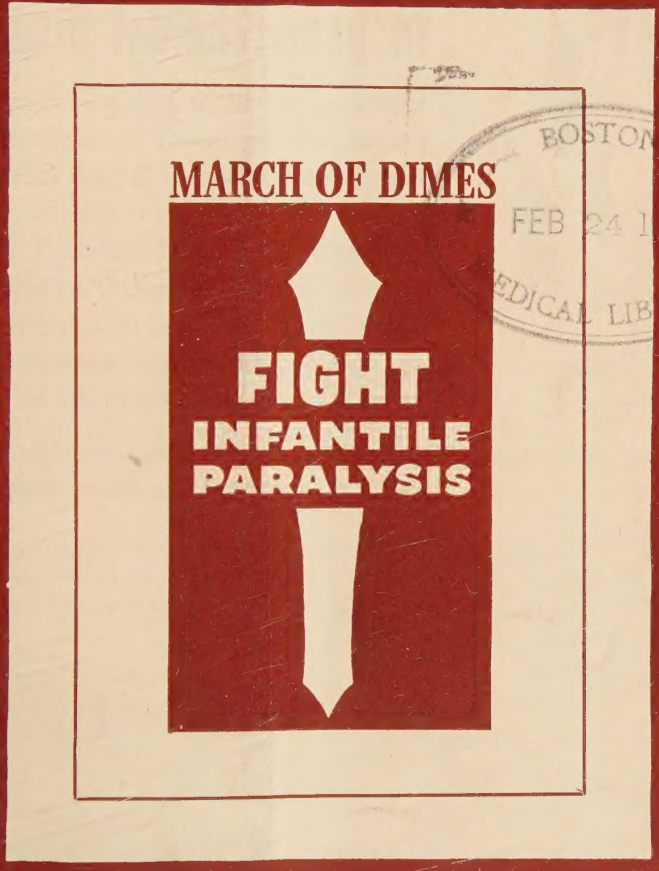
MEDICAL RECORD



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Vol. 160, No. 2

in hemorrhoidal disorders

Education in itself is a slow process. Education of the patient suffering from a hemorrhoidal disorder in the use of local medication is both difficult and slow. For the patient invariably stops the medication when symptoms are relieved, although complete recovery has not yet been effected. To facilitate complete recovery in hemorrhoidal disorders the patient should be "educated" to continue treatment for three to four weeks after the acute symptoms are relieved.

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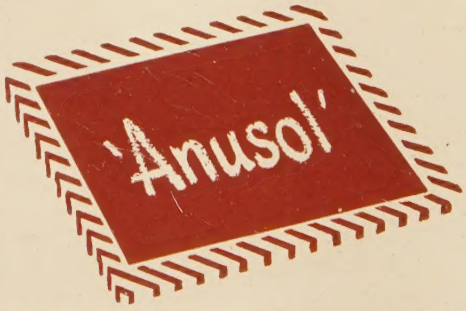

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Inositol	5.0 mg.
Folic-acid fractions	10.0 mcg.

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Cawthorne, T.: The Treatment of the Common Cold, Clin. Sup. to King's College Hosp. Gaz. 18:iii.

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FEBRUARY, 1947

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Cancer Research Projects

It has been announced by the United States Public Health Service that grants-in-aid amounting to approximately two hundred thousand dollars have been recommended by the National Advisory Cancer Council for the support of cancer research projects in twenty-one universities, hospitals and research institutions. The variety of projects covered by the grants illustrate the complexity of the cancer problem and the many angles from which research must be carried on to solve it. The projects include: Radioactive isotopes in the study and treatment of leukemia and related diseases, under the direction of Drs. Sherwood Moore, A. L. Hughes, E. H. Reinhard, and Carl V. Moore, Washington University, St. Louis, Mo. Grant: $15,000; research in gastric cancer, under the direction of Dr. Leon Schiff, University of Cincinnati, Cincinnati, Ohio. Grant: $13,000; the relation of cellular injury to the development of repair and neoplastic tendencies, under the direction of Dr. Valy Menkin, Temple University, Philadelphia, Pa. Grant: $10,000; the relation of high and low protein and calorie diets and specific amino acid deficiencies and excesses to the incidence of induced cancer in rats, under the direction of Dr. W. F. Dunning, Detroit Institute for Cancer Research (Wayne University), Detroit, Mich. Grant: $6,300; the development of inbred strains of rabbits for use in cancer research (at present such strains are not available), under the direction of Dr. Paul Sawin, Jackson Memorial Laboratory, Bar Harbor, Me. Grant: $5,650; studies on the mechanism of resistance to cancer, under the direction of Dr. John G. Kidd, Cornell University Medical School, N. Y. Grant: $14,154; the study of the variations of the Golgi apparatus in human neoplastic diseases, under the direction of Dr. Albert E. Bothe, Jeanes Hospital, Fox Chase, Philadelphia, Pa. Grant: $2,957.50; genetic and correlated studies of normal and atypical pigment cell growth, under the direction of Dr. Myron Gordon, New York Zoological Society, N. Y., N. Y. Grant: $8,620; an attempt to identify precursor groups of gastric cancer, under the direction of Dr. Owen H. Wangensteen, University of Minnesota, Minneapolis, Minn. Grant: $8,900; chemotherapeutic studies of cancer, with special attention to leukemoid tumors, under the direction of Dr. Allan D. Bass, Syracuse University, Syracuse, N. Y. Grant: $10,000; serology and tissue immunity studies in normal and cancerous mice, with special reference to the use of malignant cell strains originating from normal cell strains in tissue cultures, under the direction of Dr. Reuben L. Kahn, University of Michigan, Ann Arbor, Mich. Grant: $19,000; and, investigation of pathological aspects of gastric cancer and related lesions, under the direction of Dr. Shields Warren, Harvard University, Boston, Mass. Grant: $9,684.

The grants were recommended at the council's thirty-second meeting which was held November 8th at the National Cancer Institute, Bethesda, Md., and presided over by Dr. James A. Crabtree, acting surgeon general of the U. S. Public Health Service.

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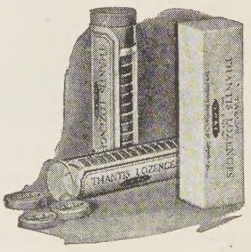

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Open Forum

MEDICAL CARE

RAYMOND TICE, M.D.
Quakertown, Pa.

"No one complains without cause and everyone has a right to medical care". This quotation seems to consummate the mental attitude of the old fashioned country doctor, so for a few minutes let us be retrospective and view him as he practiced medicine fifty years ago. His interest and patience with each one's story led people of all walks of life to consult him freely. His sincere efforts, together with his untiring attention, portrayed him as a person who was practicing a profession. They saw that he was propelled by the same stimulus which prompts a pianist to practice many months for one fine performance and then prepare for another. They noticed something within him, compelling him to proceed from day to day, much as an artist does to complete one canvas and then another. What caused this? There is no comparable word to define this quality, but to him it made the practice of medicine an art, a science and a profession. It gave him the opportunity to express his personality in his work of service. His thorough belief, that everyone had a right to medical care and the fact that he turned away no one who came to him for aid, made him appear as a "poor business personage." His belief that rendering service first would always bring appropriate compensation, perhaps substantiated this picture in the minds of the local financiers. In reality, however, he was the true sculptor who first made his image or statue and then sold it. He was beyond question or reproach, except to those who knew nothing of and had never experienced the stimulus that this man constantly felt.

This is truly the practice of medicine, and it is still our concept. We still believe that it is abnormal to complain of ill health. We know that where complaints or symptoms persist, there must be a cause. We know that the first part of the opening paragraph is not an optimistic statement in medical utopia, rather it is a truism. This same man, after months of investigation, and perhaps often on the verge of self-disgust, would not permit himself to apply a meaningless medical term, in place of a true diagnosis, and thus satisfy his patient and himself. He continued to study and search, and he realized that to apply a word, frequently ending in "emia" or "osis", would only prescribe a mental placebo for himself and no diagnosis for the patient. He knew from past experience that time frequently clarified his vision and accentuated all of his senses. How true would this axiom have seemed, had he had the conveniences of modern laboratory aids. Imagine how gratified he would have been to have been able to understand the man with hypoglycemia, to have proctoscopic examinations and x rays explain why an abdominal pain precedes a change of the stool in carcinoma of the sigmoid and rectum, to be able to see chemically, that in severe diabetic acidosis, as a result of glycogenesis and diuresis, the potassium levels might be lowered to a degree of endangering life and finally, the laboratory could teach him to be circumspect in cases of the Rh negative principle. Surely the doctor, in his periods of mental inventory, would have found a huge balance to convince him in his theory that there is a cause, whether mental or physical, and he must search for a diagnosis and abstain from using loose terms. His picture has won first prize—he has been compensated! He is happy and allows himself to comply with his urge. He knows that he is on the positive side of life and the forces of the negativism are completely overwhelmed. Or are they?

Just as delighted as he would be to see the advances, diagnostic aids and discoveries in modern medicine—he would be much amazed to find that nonmedical groups no longer mention the first half of his quotation and everything written and spoken of today pertains to the latter, i.e., everyone's right to medical care. He would be astonished beyond words to learn that the thought of many is, not how much good is, and has been done—but "what does it cost?" He would be unable to understand why the commercial side of medicine is receiving this prominence. If he were to learn that much of this was an outgrowth of a group who set out to investigate the per capita cost of medical care, he would ask, "why do they not foster a similar idea, to investigate the per capita cost of legal care?" He would undoubtedly recall months of surgical care and worry over some accident case which was followed by his testimony in court. There, he would present a bill, which when compared to half the verdict rendered or half of the damages received, would make him feel ridiculous. He would further compare legal and medical charges and would again say "why not a comparison between the per capita cost of medical and legal care?" He might go further and wonder if it ever dawned upon those who like to investigate per capita costs, that much time and money could be spent on per capita cost of government, hidden and other taxes, lend lease, subsidies, and war surplus and cost of investigating costs. These thoughts might consume a great deal of time for him and present many interesting and enlightening tangents, but eventually he would return to per capita cost. He would ask himself, "I wonder why they never figured the per capita cost of sanctimonious care? Wouldn't it be a good idea to figure comparative costs including movies, smoking, cosmetics, sports, amusements, clothing, provisions and foods, dues, tips and so on?" He might visit our large clinics, our hospitals and dispensaries, our city practitioners as well as the present country doctors and there, I believe, in the great majority of cases, he would find that they sincerely believe "that everyone has a right to medical care" and that they are, and have been administering it. He would, however, notice that much stress is laid on the latter half of his quotation. The political bodies would have us think first of compensation, triplicate forms and control

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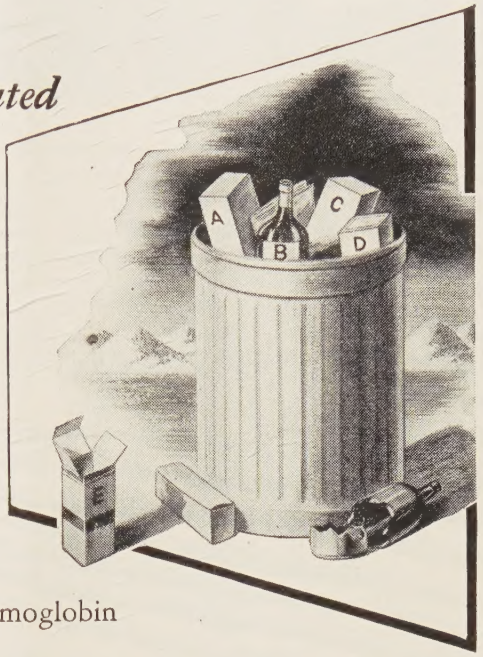

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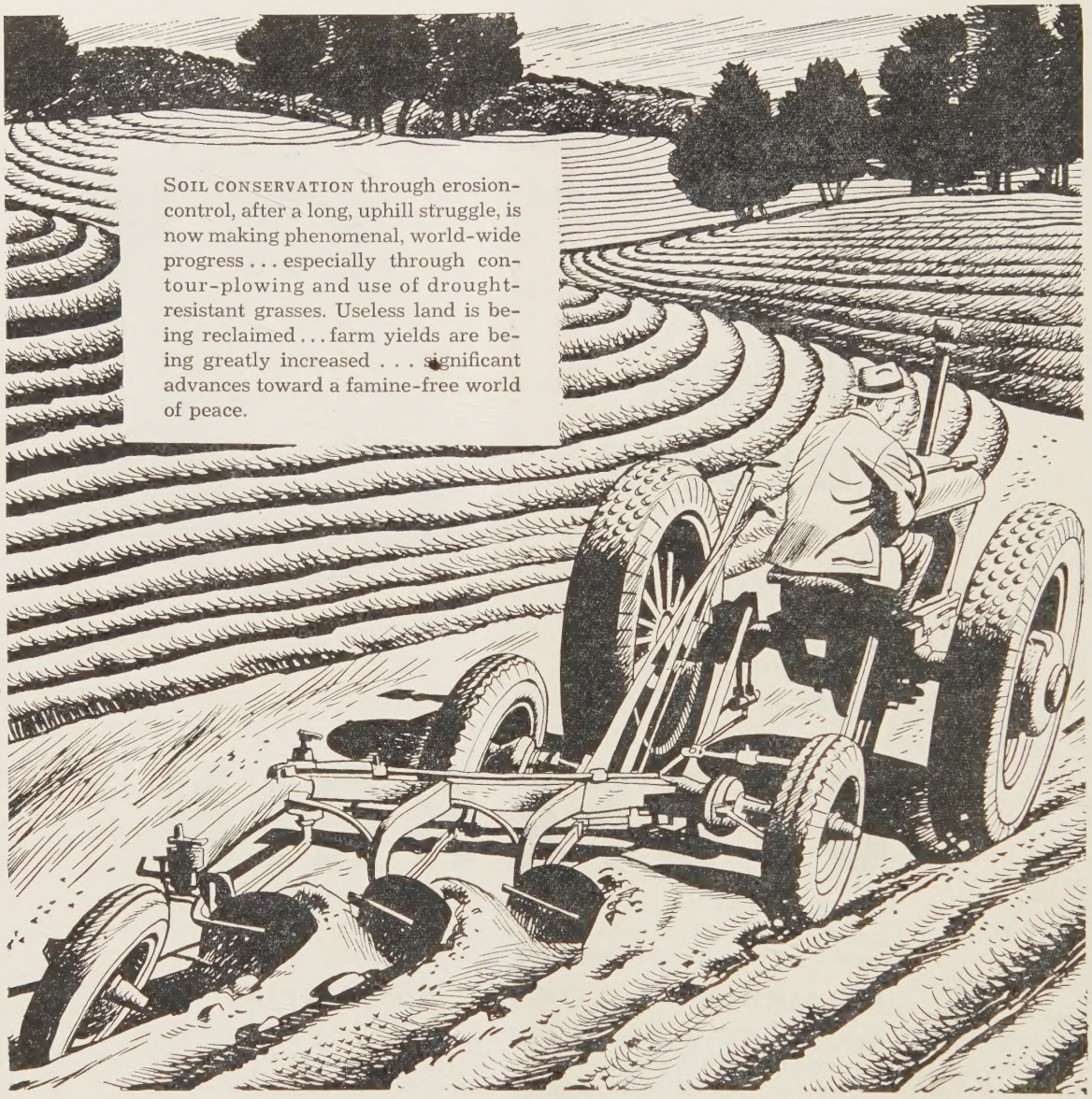
Toward a Better World



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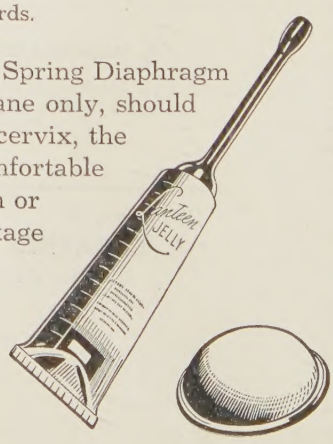

Lanteen

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boards to verify costs. He might notice that there has been a frequent tendency to think that each and every patient must first be accounted for by an agency and a good financial rating. He might overhear some political or social worker instruct a patient to visit a doctor and guarantee him that the doctor would be well paid for services rendered.

Truly, would he exclaim at the end of his tour "what complicated complications!" Whose way of practice do you think he would choose? This man who has always been trained to think in these terms of remedy and cure, I believe, would again think thus—he might look upon us as though we were infested with some political malignancy and would surely think in terms of diagnosis and cure. He might admonish us to continue the practice of medicine as an art, and insist that we compel comparative study. In addition, he might warn us that it would be better for us to receive thanks for the care of the indigent, rather than have it devoured by a political or social benefactor. He would certainly reread to us his quotation "no one complains without cause and everyone has a right to medical care", and he might ask all of us to repeat it to ourselves daily for a period of one month and then refill the prescription. Indeed, I am sure of one thing that he would make a point of telling us, and that is, "A severe malady is threatening you and your organization. Do something about it—don't just talk of it! Be big enough to rapidly frame, adopt and institute a cure or plan that will be just as fair to the patient as to yourself. Talk alone will not suffice! Such a plan must and will win. There can and should be no procrastination! Don't delay your therapy for this malady, and watch it carefully as it is administered." He would undoubtedly quote to you "It is now or never that the support of a united profession is demanded. If the Medical Service Association of Pennsylvania contract still has faults, it behooves us to work from within for their correction, rather than stand aloof and criticize from without. With the firm, united, enthusiastic backing of the profession, medical service insurance should not have any further difficulty in its rapid expansion." He would tell you that this was quoted from an article which appeared in the August issue of the *Pennsylvania Medical Journal,* by Dr. William Estes Jr., president of the state society. He would advise you all to read or reread it, as it is proof that our officers are doing their utmost in this crisis. He would admit that he has often asked himself why there must be an intermediary body of control? Why couldn't the physicians be underwritten by the state society and the American Medical Association and then they collect the monthly premiums and render the treatment? He would wonder whether this would not expedite a plan to care for house and office calls. He would read to you Dr. Estes' conclusion to his article, i.e., "in describing a few of the public health problems upon which present trends are focusing attention, I have been attempting to indicate the responsibility of the medical pro-

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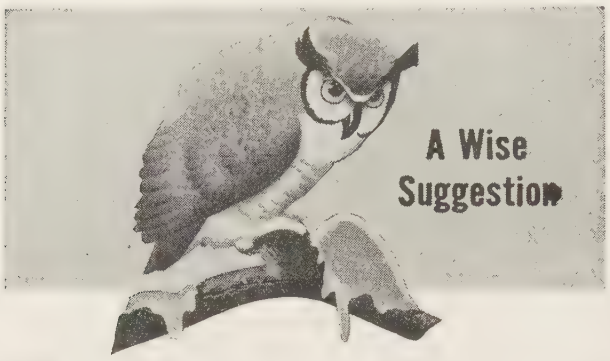

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fession to the public, collectively as well as to our patients individually. This obligation should be accepted fully. To meet the menace of this economic threat, the power of the State Medical Society must be used in every field to indicate that the profession itself is girded with full armor to lead the battle for better health."

Our country doctor has, I believe, given you the diagnosis. It is "Political, Collective, Individual Confusion" or "Centralizationism 'Grand Mal'." He has given you the treatment. In outline it is as follows:

1. Pick your drug, administer it boldly and watch its action. 2. Talk about the cure, not the disease. 3. Treat the entire disease, not part of it. 4. Practice the art of medicine, not the finance of health. 5. Support the officers of your medical organizations, give them your views and urge them to complete as simple a plan as possible. "Red tape makes blue moments!"

We have mentally visited with our colleague of a half a decade ago. He would be more pleased if you thought of this subject in the next few weeks to come, than if you entirely agreed with him at the present.

Third and Juniper Streets

Army Institute of Pathology

Appointment of twenty-four eminent scientists as resident consultants and scientific advisory board members to the Army Institute of Pathology, Washington, D. C., has been announced by the war department. In keeping with the medical department policy to fully utilize the experience of outstanding men in the various fields of scientific endeavor, the surgeon general, United States Army, has appointed a scientific advisory board to consult in the reorganization and operation of the Army Institute of Pathology, the central laboratory of pathology for the United States Army. Most of the men serving on this board have been resident consultants to the institute, while others are outstanding representatives in the fields of teaching and research.

Members of this board will advise the director of the institute in regard to experimental research, with the view of eliminating unnecessary duplication and to the proper utilization of the vast stores of accumulated material. They will be consulted in the training of personnel, the use of new techniques, equipment and scientific apparatus and of qualified personnel for professional work. The chairman of the division of medical sciences, National Research Council, will serve as an ex-officio member of the board. This group will act as consultants to the surgeon general, United States Army, through the director of the Army Institute of Pathology. Representing an integral part of the surgeon general's proposed research center, the Army Institute of Pathology, in entering this important phase of readjustment and expansion, will utilize the advice and counsel of these outstanding men in formulating policies relative to research and training.

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Gerilac offers these nutritional values in a palatable, easily consumed and readily digestible form (suitable for use as a beverage or in Special Diets) It also lends itself ideally for the nutrition of convalescents and of pre- and postoperative cases.

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First Postwar X Ray Consultants Conference

At the first postwar conference of x ray consultants to the Surgeon General, held December 12, 13 and 14th in the Pentagon Building, Washington, D.C., the redesign of x ray equipment for use by field medical units, highlighted the discussions.

During World War II, it was the universal experience of the U. S. Army radiologists throughout the world, that roentgenological equipment shipped overseas answered the purpose for which it was intended in most cases; although local improvisations and repairs demanded much of the time from the x ray personnel that should have been devoted to technique and diagnosis. Much of the equipment obtained for rear area hospitals, was of the standard, commercial design and was not intended to be frequently moved and set up under adverse conditions, as was commonly experienced in even the largest of the overseas hospitals.

It was determined that by redesign of all x ray equipment used by field medical units, a minimum number of models of the military x ray machines, tables and auxilliary equipment would answer the demands for all radiological requirements, yet simplify the production and procurement in time of emergency and greatly reduce the demands on the supply service for spare parts and maintenance. The redesign will take advantage of recent advances in the basic designs of x ray equipment, as well as the use of lighter materials which will contribute to the overall reduction in weight, so desirable for air transportation. The development study will include the maximum use of the adaptation of packing cases for essential hospital furniture, when hospitals are operating rather than moving.

Directing the conference was Dr. Byrl R. Kirklin, Rochester, Minn., formerly a colonel in the Medical Corps, and consultant in radiology to the surgeon general. Dr. Kenneth D. A. Allen, Denver, Colo., formerly a colonel in the Medical Corps, and chief consultant in x ray for the European Theater of Operations; and Dr. Earl H. Crowder, Evanston, Ill., formerly a colonel in the Medical Corps, and consultant in x ray to the North African and Mediterranean Theaters of Operation contributed valuable recommendations, based upon their recent and prolonged overseas experiences in those theaters. Maintenance consultants for this conference were James G. Lee, Charlotte, N. C., formerly a major in the Medical Administrative Corps, and associated with the supply service of the Surgeon General's Office; and Charles S. Barron, Atlanta, Ga., who as an army captain, was in charge of maintenance in the Mediterranean Theater of Operations.

The conference was the first in a postwar series of consultants' conferences in the medical specialties, conducted by the Army Medical Research and Development Board, for the purpose of reviewing theater reports and obtaining recommendations from the most outstanding authorities for the improvement of equipment so necessary to maintain the department planning program abreast of current trends.

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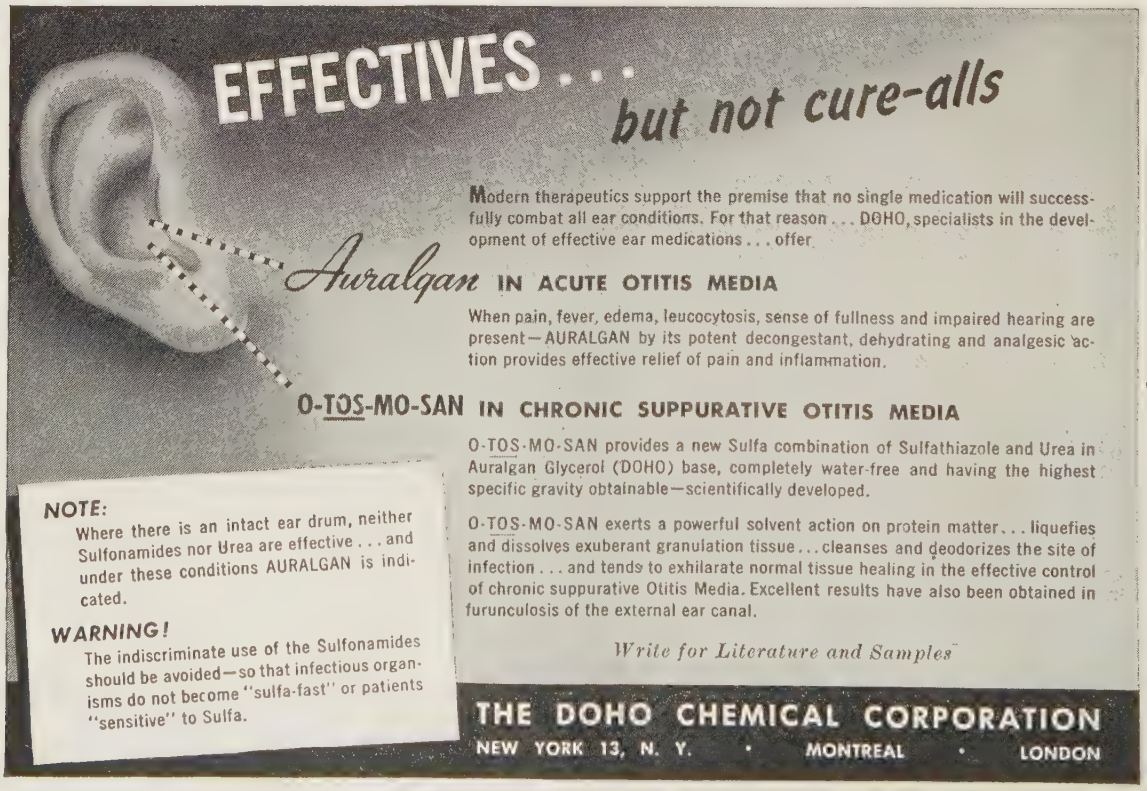
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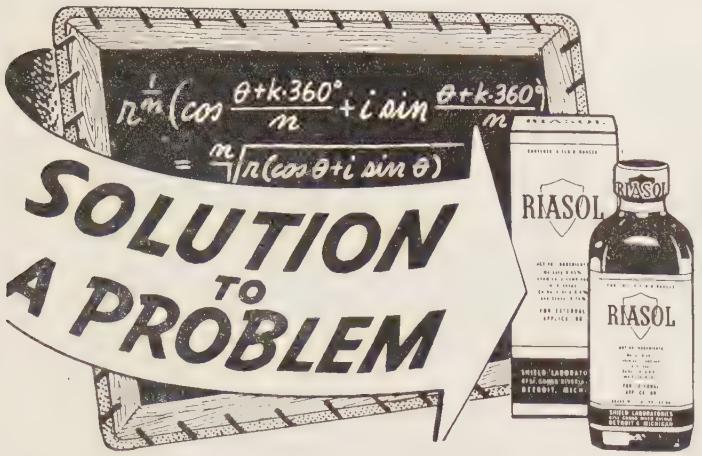

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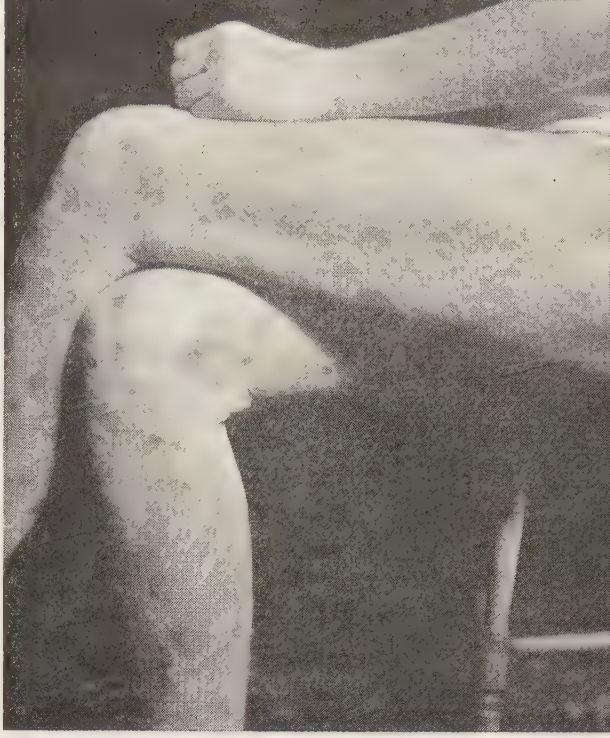

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Army Report on the Use of Streptomycin

According to the report of the Surgeon General's Office from the Halloran General Hospital, the new antiinfection agent, streptomycin, which is in the same general class as penicillin, appears effective in appropriate doses against more than half the infective bacterial organisms ordinarily encountered by surgeons. Clinical studies of the use of the drug throughout the army, have been submitted and evaluated at Halloran. On the other hand, it apparently has specific poisonous effects when given over an extended period, and bacteria soon become resistant to it so that it probably can be used only once, with maximum effect, within a limited period on the same patient.

Army experience with the drug is probably the most extensive to date, due to its ability to compile and follow results. Outside the services, because of limited opportunities to observe results in large numbers, there have been varied, and sometimes quite exaggerated, reports on its value and it is often popularly referred to as a "miracle drug." Some of the first careful observations of its effects have been carried out by army doctors upon orders of the surgeon general, and these are being continued. The findings to date are summarized in the *Army Medical Bulletin,* November, 1946.

The observation on the ability of the bacteria to develop resistance to the drug after a few days, may be of particular importance at this time. The same has been noted in respect to both the sulfa drugs and penicillin, but apparently the phenomenon is more pronounced with streptomycin. In at least one case, test tube experiments showed that there was a one hundred-fold increase of the resistance of an organism in ten days. Given indiscriminately, the drug may lose all value for a particular type of infection in an individual for the rest of his life. Improper use may cause variation and selection in disease agents, so that streptomycin is no longer effective for the infection where it is of greatest value at the present time. Of paramount importance, is the determination whether a specific microorganism is susceptible to the drug before it is administered by mouth, by injection or direct application.

The army experience bears out previous claims that streptomycin is of especial value in clearing up infections of the urinary tract, provided that the organisms causing the infections are susceptible ones. If the treatment is not entirely effective in three days, ordinarily no good results can be expected from its continuation. In gonorrheal infection, which has proved resistant to both sulfadiazine and penicillin, outstanding results have been obtained. Use in army hospitals gives no support to claims that the drug is of value in infections of the prostrate. The drug is not concentrated in that organ. It was found to have very little value against bone infections, except when used in conjunction with surgery where there could be direct application. Thus far, streptomycin has not given dramatic results in peritonitis, but its continued use as an auxiliary treatment seems justified. In various dysenteries, due to susceptible bacteria, considerable benefit has been noted, sometimes when the drug is given by mouth alone. In septicemia, provided that the organism responsible for the infection is a susceptible one, streptomycin has proved very effective, but it is still essential that unapproachable foci of infection be removed by surgery. The substance has little value, so far as the army experience goes, against typhoid fever and it is apparently of no use in controlling carriers of this disease.

In undulant fever, there have been apparent clinical arrests of the infection from the combined use of streptomycin and sulfadiazine, after each drug given alone, had failed. Further study will be required, however, before any valid conclusions can be reported. It is very effective against tularemia, or rabbit fever, provided that the specific organism responsible, has been demonstrated in test tube experiments to be susceptible to the drug. Up-to-date experience with only a few cases of meningitis have been reported and the results, in conjunction with other treatments, have been quite good. The army doctors found, however, that it must be given by injection into the space between the thick membranes surrounding the brain and spinal cord and the brain or spinal cord tissue. Circulating in the blood stream, it cannot pass this barrier to reach the infecting organisms.

Excellent results have been obtained with direct application of the drug to infections of the external ear, the pleural cavities and the brain. Infections elsewhere will not reach local foci of infection in sufficient concentrations to be effective. One of the hopes of the medical profession has been that streptomycin would prove of some value against tuberculosis. The army experience neither confirms nor refutes this, since a much longer series of investigations will be required before there can be any valid conclusions.

Balances against the demonstrated value of streptomycin in suitable cases, are some apparently toxic effects. Some of these are probably due to impurities in the drug, but others seem to be specific for the drug itself. The most serious of these, is what seems to be an irreversible damage to part of the eighth cranial nerve. This appears when streptomycin is given in large doses by injection for more than ten days. This means that one's sense of balance may be disturbed for a long time, with possible attacks of dizziness and nausea. This was found in two army cases. A third patient showed partial deafness, indicating that there had been a poisonous effect on the other portion of the eighth cranial nerve, which is the path of hearing. Toxic effects were also noted on the kidneys. All this demonstrated that the drug should be given only by physicians, and then only after careful consideration has been given to the organisms involved and the safe dosage.

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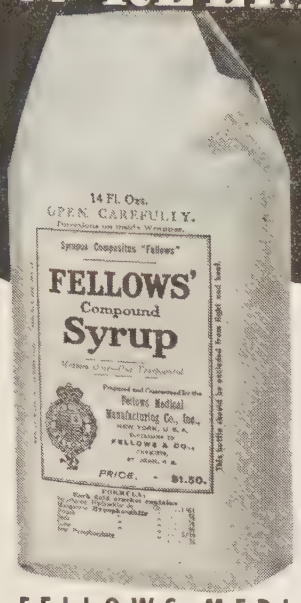

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TOXIC AGENTS IN THE GENESIS OF PELLAGRA AND PELLAGROID*

R. de R. BARONDES, M.D.

Los Angeles, Calif.

Pellagra has generally been ascribed to a lack of sufficient pellagra-preventing substances in the diet, but the factors underlying this deprivation are many and various. In spite of extensive study, a complete understanding of the etiology is still forthcoming. As early as 1776, Venice passed legislative measures prohibiting the sale or exchange of all ill-smelling, ill-tasting and discolored corn, believing it to contain a toxic substance which was responsible for the disease. Pellagra, however, existed in Europe before the sixteenth century, when corn for cultivation purposes was imported from the Americas. About ten years ago, Goldberger and others reported that the nicotinic acid of the vitamin B-complex was found to be clinically effective against the pellagra symptoms in man, and black-tongue in dogs, and believed that the lack of this component was the causative factor.

Some do not believe that a deficiency of some essential nutrient agent is the main etiological factor, but hold that a toxic agent is responsible for the symptoms of pellagra (1,2,3,4,5,6,8). This view now seems further substantiated by the recent findings of Elvehjem, Hoehl, Tepley and others (7) who noted that a diet of corn exerts a pronounced retardation of growth in rats which is counteracted by nicotinic acid. They believe that corn contains some relatively indigestible substance which combines with the dietary nicotinic acid so as to prevent its absorption from the digestive tract. This is likened to the effect of the avid protein, avidin, an indigestible factor in eggwhite which has a specific affinity for biotin and thus there results a lethal biotin starvation. Be that as it may, this would not explain the development of pellagra in those people where corn never appeared as an item in their diets.

Why pellagra should become so prevalent, even on the increase, when the knowledge of vitamins and nutrition is now so well understood, remains unexplained (1). Statistics show that over thirty percent of large groups of hospital patients die, or go into a chronic progressive illness, in spite of what appeared to be ample opportunity for the vitamin therapy to have been effective. This rather poor showing would point to a cause other than one of a nutritional deficiency. In our Southern states, where there is a large rural population of the poor laboring class, pellagra would be expected; but in the adjoining countries of Mexico and Central America, and also in the Orient where rice and not corn is eaten, the economic and social conditions of the poor being even worse than our own potential pellagra population, there is comparatively little pellagra to be found. If a mere deficiency of any food factor was the basic causation, this disease should be far more common, the diet being in no way worse, except that corn or rice is eaten. The Mayan Indian lives almost wholly on "one dish" only, seventy-five percent of which is corn, yet neither pellagra nor beri-beri prevail there. The Oriental, and of late our own prisoners-of-war, subsist mainly on a diet of white rice, but pellagra does not develop although the vitamin, protein and fat value of rice is much lower than that of corn. However, beri-beri is a common complaint. Pellagra is rare in beri-beri districts, even though the toxic agent is apparently absent in the diet, and the pellagra-preventative factor in the small amount of fish ingested may be sufficient to ward off development of the disease. With the present shortage of foodstuffs now generally existing throughout the world, the soil for the development of nutritional disease is ready for planting, for many will be living on diets well below the nutritional level.

In previous publications (2,3,4,6,10), the fact was pointed out that there is more than one etiological type of pellagra, and more than one precipitating factor. To correct certain fallacies and misconceptions concerning pellagra, some of its complexities should be better understood. The pellagra syndrome can result from: 1. A toxic or adverse agent in the diet; 2. a deficiency of some essential food factor; 3. or some body abnormality or metabolic disturbance that interferes with the assimilation and utilization of dietary essentials. In such diseases as pellegra, pellagroid, acrodynia, black-tongue, xeroderma, lathyrism, sprue, etc., the ingested food has been known to contain such toxic agents as cyanic glucosides, and cyanogenetic substances (2,3,4,5,8). These toxic agents, when in the body, inhibit the

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respiratory mechanisms of the tissue cells, suppressing oxidative processes, and interfere with the utilization of food essentials so that more or less irreparable tissue damage occurs (2,5).

Incidence

Pellagra is known to result when corn, maize, yams and other food plants are eaten in a decayed state, or if they are grown in a climate which does not permit them to become fully mature. One of the main toxic agents found in these foodstuffs is a cyanogenetic glucoside dhurrin that yields prussic acid upon hydrolysis. Cyanogenic substances are also found in molasses, sorghum, peas, beans, tobacco etc., all used to some extent in the pellagrous districts. Prussic acid is concerned in some manner in the building-up of the protein molecule, since HCN in cereals and vegetables decreases in amount as the protein content increases with the process of ripening. Furthermore, the toxicity of cyanogenetic plants varies greatly according to the temperature and humidity of the climate, and with agricultural conditions such as the soil, moisture, manuring, tillage, etc. (5). These geographic and climatic characteristics under which the biological activities of the plants develop, offer a partial explanation of the development of such diseases as pellagra. The stage of maturity, in the case of the grains, seems to be the greatest factor in the variation of toxicity; acute poisoning with sometimes fatal termination occurs in animals when unripe grain is eaten. This does not occur when the grain is fully ripe. The shrub known as sweet cassava, a common food in West Africa, contains less cyanogenetic glucoside than the bitter, but the degree of toxicity is found to be reversed when the former is grown in a very dry soil and the latter in a fairly moist one. On such a diet, pellagra is rife. All cyanogenetic substances inhibit oxidation when taken into the system. They inactivate the vital enzyme systems and cause irreparable tissue damage to such detoxifying organs as the liver and adrenal gland. Not only is prussic acid highly toxic but it definitely inhibits growth and calcification, and causes the lime salts to be thrown out of the system. Recent study shows that HCN is also a factor in the rachitogenic diet (8). The incidence of rickets is low among the Mayan children and elsewhere where pellagra is not prevalent; this and other calcium-deficiency states probably correlates with the HCN or cyanogenetic substances in the diet. One should be aware, however, to guard against the confusion of facts and hypothetical deductions.

No investigators to date, have actually produced diseases in animals comparable to pellagra, or beriberi, solely by omitting vitamin B-complex from a satisfactory diet. Hess and Drummond found that on feeding cyanides to pigeons, on an otherwise optimal diet, some of the symptoms of a Vitamin B_1 avitaminosis could be produced, even to bringing on an opisthotonus. The explanation could well lie in the fact that vitamin B_1 ($C_{12}H_{17}N_4OS$) contains sulfur, and its effect is destroyed when the sulfur combines with the "avid" HCN. In beri-beri, there is a marked fault in the carbohydrate metabolism which leads to the formation of glucoamines, neurotoxins and other toxic substances in the body. An accumulation of lactic acid and lowered oxidation also occurs in the brain and nerve tissues and causes various degenerative changes (2,5,9). A high, or over-rich carbohydrate diet serves to intensify a vitamin B_1 deficiency (athiaminosis). Thiamine aids the oxidation and intermediary metabolism of the carbohydrates through the lactic acid state, increasing the oxygen usage and respiration of the tissue cells. The more carbohydrates ingested, the greater is the body's demand for thiamine. This catalyst is also concerned in the prevention of edema, through the regulation of intracellular fluids and it also plays the rôle of a coenzyme in the oxidative action of the cells, e.g., the dehydrogenase systems concerned in the intermediary metabolism of the carbohydrates. The dehydrogenase systems of the brain and central nervous systems are very susceptible to the lack of oxygen, viz., the effects of anesthetics and narcotics which produce cerebral anesthesia and unconsciousness. Vitamin B_1 would be indicated in those disorders where morbid disturbances of the fluid balance, and an alteration in the electrolyte concentrations occur.

A sulfur-deficiency state (asulfurosis) also appears to exist when pellagra is present. This could result from either some body defect, or the subsistance upon a diet poor in this element. Analysis of corn shows it to be very low in cystine. Sulfur is not only necessary for body detoxifying purposes, but it also aids in cellular respiration and the increased oxygen capacity. The body can only utilize the organic form of sulfur; the inorganic form passes out of the body unchanged. Sulfur-containing bodies, those having sulfhydryl forms such as cystine, methionine, etc., are the sources of glutathione, which is most necessary for cellular respiration and therefore, life itself. All sulfhydryl compounds are essential tissue constituents concerned in the biological phenomenon of oxidation-reduction. Quite apart from the ordinary duties of the body, sulfur is called upon when emergencies arise, to combine with cyanic and other toxic substances which are ingested or that arise from some perversion of the tissues. The detoxification of the cyanic substances in the body is brought about by conversion to thiocyanate. Under such conditions, a sulfur deficiency state would eventually appear whenever the system makes any increased demands for additional sulfur in the detoxifying processes, and it would then constitute a pathological entity (2,3,4,5,6,8). A depletion of the body sulfhydryl also occurs from toxicoses resulting from the ingestion of selenium, fluorine, the heavy metals, metalloids, alkaloids, certain therapeutic drugs, etc., all of which might become the pathological basis of many physical symptoms commonly attributed to nutritional deficiency states.

All the diets found to be beneficial to the pellagrin, contain sulfur, calcium, manganese and mag-

nesium, the latter two elements apparently being required as catalysts for the stability of vitamin B-complex and the vital enzyme systems concerned in tissue respiration and metabolism. The exact *modus operandi* of the sulfhydryl in the body is not known, but we know that it does play some vital rôle in choline metabolism and the detoxifying processes of the liver.

Case History

The author presents a description of a case that might be considered a separate clinical entity, namely pellagroid, for in the absence of diarrhea, salivation, glossitis, neuritis, irritability, migraine, mental confusion and dementia, one could not establish a true diagnosis of pellagra.

The patient, a Chinese, aged sixty-five, following a gastric resection, developed certain pellagra-like symptoms over a period of one year. Just what the gastropathy was that indicated surgery, could not be determined. An interpreter stated "much stomach was cut out for pain." The condition was thought to be a gastric ulcer, although this condition is comparatively rare among the Chinese. For the past few years, the patient preferred, as a diet, decorticated rice, white bread and coffee. Occasionally he would indulge in cheap corn whisky which he admitted would aggravate his complaints. For some time previous to the gastric operation, he had been taking large amounts of sodium bicarbonate as the only medication, and he had continued to take it following the gastric operation.

The first complaint which developed after surgery, was a scaly, symmetrical, reddish-brown rash on the lobes of the ears, extending later to the cheeks, forehead, nose and back of the neck. The auditory canals became very inflamed and tender, oozing a yellowish excoriating secretion. Vesicular and bullous lesions appeared on the fingers and dorsal surfaces of the hands, progressing gradually upward above the elbows. The skin in these areas became quite thickened, desquamating severely, accompanied by a severe burning sensation. The affected parts became aggravated and quite edematous when exposed to sunlight. A similar, symmetrical-spreading dermatitis appeared later about the ankles and legs, which became more severe on the anterior surfaces. The buttocks showed large, thick, pigmented areas which desquamated severely in large patches. Vitiligo was observed on various parts of the body, being more pronounced on the extremities. The appearance of these whitish depigmented areas should always make one suspicious of a pellagrous state. The skin of the face acquired a peculiar ashen-gray color, the melanosis resembling that hue seen in argyria. It took the shape of a large butterfly and included the lower half of the forehead, orbital region, cheeks and the upper lip. A severe cheilitis was in evidence, the melanotic-colored lips showing deep radiating fissures. The lateral and undersurface of the tongue was of a purplish-red color, the rest being coated a yellowish-gray; however, there was no evidence of glossitis or salivation. The throat was slightly inflamed; the buccal mucosa and the gums where some teeth were missing, showed scattered, whitish areas which differed somewhat from that of a true leucoplakia. The nose, which was severely inflamed and denuded, was of an irregular contour apparently the result of abnormal fatty deposits from some body lipidystrophy. The hair had fallen from the top of the head and the remaining hair which was previously gray in color, assumed a peculiar bluish-gray tint. The scalp showed a goose-skin, scabrous appearance, not unlike phrynoderma which is seen in advanced vitamin A deficiency states (2,6,11). The canthi, palpebral and scleral conjunctivae, were reddened and inflamed. At times the eyelids became so edematous, that vision was interfered with; this condition was accompanied by a yellowish exudate from the conjunctival sacs which matted the eyelids together. A similar eye condition is seen in animals with distemper where an advanced vitamin A deficiency state exists (11,12). Dimness of vision was also complained of, but other than an advanced *arcus senilis*, no opacities could be discerned. There was a complaint of both a severe photophobia and an hemeralopia; these states always appear to accompany one another. A sigmoidoscopic examination revealed scattered anemic areas of the rectal and anal mucosa, the latter being aggravated by multiple radiating fissures. Further physical findings were a chronic nephritic state, porphyrinuria, hypotension, hypochlorhydria, moderate degree of anemia and lymphocytosis and a Laennec type of liver cirrhosis. (The etiological factor in this type of hepatic cirrhosis, results from both a vitamin B-complex deficiency and a hepatoxic agent.)

Comment

In this case, one would not be justified in making a diagnosis of pellagra since there was an absence of diarrhea, salivation, glossitis, neuritis, irritability, mental confusion and dementia. Whether these symptoms would have developed eventually is conjectural. It appears odd that the patient did not develop subclinical symptoms of beri-beri, since the ground work was an ideal basis for such a development. Probably advanced age is not conducive to the development of this disease, whereas it would be more likely to occur in a younger person. In view of the long continued diet of rice, white bread, coffee, alkalotherapy and the gastric resection, this patient, in fact, should have presented the clinical entities of all the deficiency states. White rice is much lower in the dietary essentials than any other basic food, while white flour has over ninety percent of its vitamin content removed in its processing (2,12). For some unknown reason, true pellagra and beri-beri, as a rule, do not develop in the same individual at the same time; at least research of the available literature describes no such case. Some factor, other than a deficiency, perhaps geogenetic, is instrumental in first precipitating these diseases. The various races, through constitutional and ethnic differences, differ in their capacity to use particular

nutrient essentials (2,4,6,11). This is noted in the limited diet of the nutrient essentials of such races as the Eskimo, Hindu, Oriental and Fiji-Islander among others. Some individuals require a greater need of certain nutritional components than can be acquired in the usual normal diet and therefore, they should be fortified for proper nutritional rhythm. Age is also a factor in disease-initiation; the younger being more susceptible, develop the signs of the deficiencies sooner than the old. Animals, other than man, are able to distinguish and sense those food-essentials necessary for their well being; this "sense", or instinct, is certainly lacking in the *homo sapien* who eats and drinks anything as long as it appeases his hunger and slakes his thirst. One cannot predict what clinical manifestations will develop in anyone who is deprived of certain essentials. These are subject to a considerable variation, such variation occurring in one individual and between individuals on the same diet.

Pellagra and pellagroid are not dermatological problems, nor is beri-beri a neurological one. They are truly systemic disturbances which in turn are the underlying causes of the local problems.

The degree of body tissue changes described in this case were correlated with multiple deficiencies of vitamins, minerals, protein and fat, these sequelâe being more prevalent than generally supposed. The hypochlorhydria apparently followed the gastric resection and was aggravated by an ill-advised unnecessary alkalotherapy following the surgery. The vitamin B-complex deficiency was also a factor, as it led to an achlorhydria and liver damage. This vitamin-complex is incapable of being stored properly by a damaged liver and the B-complex cannot be utilized by the body in the absence of the proper gastric pH, as it is unstable except in an acid media.

The pellagrous states, beri-beri, neuritides, neuralgias, etc., are benefited by components of the B-complex group only for short periods of time, and the dosage must then be increased; eventually, however, the disorders return. Why this is so, is not known. Apparently the body becomes conditioned to the various vitamins and must be augmented with larger doses, or supplied with necessary catalysts to insure proper absorption, retention and utilization. Such factors as alkalotherapy, diets high in alkaline ash and the use of alcoholic liquors exert adverse effects on the vitamin B-complex group and eventually lead to symptoms of such a deficiency. Any therapy, vitamin or otherwise, will not effect a cure where the causative factors such as faulty diets, systemic disturbances, etc., are allowed to remain unchanged. Should the body tissues be extensively damaged, no therapy could restore these structures and it would be of little benefit.

All components of the vitamin B-complex group appear to supplement one another, and should be used together with their necessary catalysts. An excess of one component, or an unbalance in the ratio between them, result in deficiencies of the others (2). If a well-balanced adequate diet is available, one containing all the nutrient essentials, then vitamin therapy would be indicated only under exceptional circumstances. The utilization of any vitamin takes place only if such a deficiency exists in the body. The current indiscriminate use and misuse of vitamin B-complex is to be deprecated.

The anemias noted in pellagra; pellagroid, pernicious anemia and sprue, among others, are correlated with faults in the stomach and liver mechanisms. In beri-beri and pernicious anemia, the cord degenerates as the result of changes in the acid-base balance, which is brought about mainly by an achlorhydria and a vitamin B deficiency or destruction (9,10,12,13,14).

The dermatitis, melanosis, histamine localizations and hematoporphyria are related to the adrenal injury following the failure of the liver to properly detoxify certain toxic substances in the body; though some of these were initiated by the multiple vitamin deficiency. Vitamin B aids in restoring function to the partially damaged liver cells, which are then able to cope to some extent with the toxic agents responsible for the disorders. For proper maintenance and activity of the adrenal gland, vitamin C appears to be a necessary requisite. In a deficiency state, the body may synthesize ascorbic acid from the hexoses. Heavy doses of vitamin C and sodium chloride, cause a more or less depigmentation of melanin in the skin of a patient with Addison's disease. When melanin is slightly oxidized, it turns a reddish-brown such as the color noted in pellagro-dermatitis. Melanin is primarily derived from tyrosine and phenylalanine. Under certain abnormal conditions in the body, these aminoacids may be oxidized and will yield as high as one percent HCN, and other toxic products. Certain dairy products such as milk and cheese are rich in tyrosine, and when undergoing decomposition in old and stale products, they release a cyanic substance. (Other such toxic agents as guanine, $C_5H_5N_5O$, and closely related end-products of protein degradation in experimental animals, produce typical symptoms of a vitamin B_2 deficiency. Whether this is due to an adverse systemic effect, or is the result of an avid-binding of the vitamin, is, as yet, not known.) The latter is thought to be one of the precipitating factors in the pellagra picture, as is noted in such countries as Rumania and Italy (2,3,5,8,15). Tyrosine and phenylalanine are related to such hormones as thyroxine and epinephrine, which act as catalysts to increase the oxidative processes of the tissues. Epinephrine is antagonistic to both insulin and histamine. Should damage occur in the adrenal gland, control over the histamine could not take place properly, and a vicious cycle then ensues which causes further adrenal injury. Histamine causes fluid cell ingress and is a severe skin irritant, producing dermatitis and edemas of various sorts. This amine lowers the pH of the normal gastric secretion when injected parenterally or through sunburn, when the histamine substance liberated in the skin, is absorbed by the blood. Histamine acts to increase capillary permeability, permitting the escape of plasma into the tissues and causing stagnation in the en-

larged capillary bed. This substance is a precipitating factor in certain neuropathies, pellagrodermatitis, erysipelas, the exanthemata, herpes zoster and the nutritional edemas of beri-beri, etc. A similar-acting skin irritant is hematoporphyrin which results in vesicles and bullae. A porphyric state may result from either a deficiency, a fault in metabolism or a toxicosis. The porphyrins, bile pigments, and other photocatalyzing and photodynamic substances render the body acutely sensitive to light. Injections of the porphyrins stimulate the hypophysial secretions of the melanophoric and gonadotropic hormones (2,3,4,10,14).

The presence of toxic agents in foodstuffs leading to gastric, hepatic and adrenal damage is considered in the genesis of pellagra, and the significance of the observations with reference to the pathology of the lesions in pellagrous states is discussed herein. There is an intimate gastro-adreno-hepatic relationship in the maintenance of the body's well-being. The study of the detoxification processes shows the importance of systemic disturbances in the beginning, and the development of the morbid processes. Through a failure in the body's detoxification mechanisms, many systemic disturbances result, which may be confused with the symptoms of the disease attributable to other causes. The highly toxic HCN appears to be an etiological agent in pellagra, pellagroid and rickets. Cyanic substances definitely inhibit growth, calcification and cause lime salts to be discarded from the system. Through the presence of these toxic agents in foodstuffs, or those derived from faulty metabolism, concentrations of HCN may reach high levels and seriously interfere with the delicate respiratory and enzyme systems of the tissue cells. It would be unwarranted though, to consider that the mere presence of a toxic agent proves any etiological relationship to such systemic diseases as pellagra, beri-beri, pernicious anemia, sprue, rickets etc., without further proof. Thus, conclusions cannot be based upon this factor alone, without further clinical experimentation.

An asulfurosis also appears in the etiological set-up of pellagra and allied states. A state of sulfhydryl inadequacy results when it is called upon to neutralize toxic substances in the system, or from excess elimination through some body fault. The preliminary data obtained in such studies justify the continuation of work along these lines, in order that the clinical value of sulfur therapy and corrective measures may be fully ascertained.

As there is still much to be learned about the etiologies and diagnoses of the nutritional-deficiency states, the treatment of necessity will be more or less experimental, supportive and individualized. The speed and extent of a cure are subject to considerable variation, such variation may occur in one individual and between individuals under similar circumstances. Unfortunately, in spite of our knowledge of therapy and preventive measures, the results are not uniformly good; in some subjects the course of these diseases is apparently little altered by any mode of treatment.

Treatment

The purpose of this paper is not to discuss the treatment of the deficiency states; however, in the therapy of this case of pellagroid, several interesting observations were obtained that may have considerable significance. It was found that when vitamin B-complex, alone was prescribed, it not only was of no benefit, but appeared to be definitely harmful, even to causing the recurrence of the symptoms. The question was then raised as to whether vitamin B-complex was not only harmful in the presence of severe hepatic, gastric and adrenal damage, but might it cause further injury? In certain disorders, thiamine for instance, precipitates a downhill course in the toxemia of pregnancy. This could be the result of the affinity of thiamine for histaminase, its properties then being inactivated, and the biological action of this enzyme becoming inhibited, results in a destructive concentration of histamine in the body.

Clinical improvement was obtained in this case of pellagroid when the diet was changed to include liver, kidney, lean beef, fish, eggs, milk, cheese, vegex, pablum, fresh fruit and vegetables. (These foods contain the optimal amounts of all the vitamins, minerals, protein, fats and other essentials.) The water from the cooked greens was also prescribed, since much of the water-soluble vitamins are lost through cooking. Hydrochloric acid and pepsin were given at mealtimes to correct the hypochlorhydria and to insure absorption of the nutrient essentials. This was also supplemented with vitamin A and Cortalex, a preparation of the adrenal cortex which is essentially free of epinephrine and contains vitamin C which is known to be of great subjective benefit in adrenal insufficiency. Lextron which contains vitamins B_1 and B_2, and liver and stomach concentrates, proved of considerable therapeutic value when given with the hydrochloric acid and pepsin. The knowledge of such complimentary actions may be clinically important, and study of these dietary variables should be pursued (2,3,4,6, 10,11,13,15).

Evidence points to a factor, other than any known component of vitamin B-complex, in the stomach tissue and the liver; the absence of which is concerned in the etiology of pellagra, pernicious anemia, sprue, etc. (2). It may prove to be a gastric enzyme, or a coenzyme requiring the proper gastric pH and liver principle for its activation. The recovery and identity of this X-progastrin factor, "gastrinase", for want of a better term, should not be beyond ingenuity, and its use in certain deficiency states would be indicated.

In the hypoproteinemia usually existing in pellagrous states, aminoacids, administered intravenously, would maintain the nitrogen balance and restore the disturbed electrolyte equilibrium. A word of caution is injected here regarding this new form of therapy, for the reason that a damaged and poorly functioning liver cannot properly conjugate such administered aminoacids, and would probably lead to a severe acidemia, sudden lowering of the blood pressure, asphyxia, coma and a possible heart block

(12). If such an hepatic defect is suspected, liver function tests are indicated previous to any intravenous administration. The main adverse effect to be expected here, i.e., the acidemia, is not due so much to the diminished ability of the blood to carry oxygen, as it is to its lowered ability to carry carbon dioxide, which is caused by the depletion of the fixed alkali (12).

If any systemic disorder is the result of an error in diet, little beneficial effect could be expected from any mode of therapy, as long as the dietary defect remains unchanged. When extensive damage has occurred in the body's vital tissues and is beyond nature's repair, then no dietary or therapeutic measure would be likely to restore structures so injured, and would be of no avail.

The prognosis in the case of pellagroid discussed herein, was only fair in view of the advanced age, the gastric operation with the removal of considerable tissue, and the more or less damaged and dysfunctioning liver and adrenal glands. However, after approximately six months' intensive hospital treatment with careful supervision, excellent progress was obtained, although a permanent cure was neither effected nor expected. The acute lesions, i.e., those that developed later in the disease, were the first to heal; while the chronic ones, those involving the face, ears, neck, eyes and extremities, were more refractory to treatment. The cheilosis, dermatitis and melanosis, returned on such slight provocation as for example, exposure to sunlight, failure to follow the prescribed medication, resumption of the former carbohydrate diet and the indulgence in corn whisky. Perhaps there is some specific toxic agent present in liquor made from corn products that is not found in rye and other grains that has a nicotinic acid-binding effect.

Conclusions

Conclusions are always questionable when based upon the realm of probability, but a summary of the evidence shows:

1. One cannot predict what clinical manifestations will develop in anyone who is deprived of certain nutrient essentials. These are subject to considerable variation, such variation occurring in one individual and between individuals on the same diet.

2. Any factor, physical or chemical, that interferes with the proper metabolism of the essential nutrients, would eventually lead to the symptoms of such deficiency states.

3. The pellagra syndrome can result from either a deficiency of the pellagra-preventive factor in the diet, or its nonassimilation or utilization in the body.

4. Pellagra and pellagroid are two separate disease entities, being sufficiently distinct in their symptoms to warrant the use of separate terms. The term pellagra, would be reserved for the state resulting from some faulty physicochemical process, or toxicosis, that interferes with the proper absorption and retention of the pellagra-preventing substance. Pellagroid would indicate the state resulting from some systemic disorder such as gastric, hepatic or other tissue damage which prevents utilization of the pellagra-preventative factor.

5. Among the toxic agents that have been incriminated in the etiology are guanine and related protein-degradation products; also the cyanic glucosides and cyanogenetic substances in foodstuffs which, on hydrolysis, yield HCN. Such toxic substances adversely affect certain vitamins, interfere with the delicate respiratory and enzyme systems of the tissue cells, inhibit growth and calcification and cause the lime salts to be discarded from the system.

6. Pellagra-producing diets are poor in sulfur, tryplophone, cystine, manganese and magnesium; the latter two being necessary catalysts for the stability of the vitamin B-complex group and the body enzyme systems. Sulfur aids in cellular respiration and is vitally concerned in the body detoxifying processes. Diets that contain toxic substances and are low in sulfhydryl, for example corn, would further aggravate a sulfur-deficiency state.

7. Present in the stomach tissue, probably originating in the pyloric glands and perhaps also the liver, there is an unidentified pellagra-preventative factor of enzymic nature. It is not related to the vitamin B-complex group, the absence of which or its inactivation, precipitates certain manifestations of pellagra, pellagroid, sprue, pernicious anemia, etc. These symptoms can be controlled by stomach-liver concentrates when given with pepsin-hydrochloric-acid combinations.

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VITAMIN E IN HEART DISEASE

I

The Anginal Syndrome†

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In previous publications (1,2,3,) the authors have described the clinical results which were achieved following the administration of vitamin E in large doses to cardiac patients. The present paper will give a description of results obtained in an unselected series of eighty-four consecutive cases. All of these cases manifested anginal pain as one of the major symptoms. It will be seen that many etiological types are included and all degrees of functional impairment represented, from the simple anginal syndrome to congestive failure with pain.

Case Histories

Case	Sex	Age	Etiology	Major signs and symptoms	Duration	Initial tolerance	Previous therapy	Present therapy*	Results
1	M	68	H&C(1)	Pain. Dyspnea. B.P. 170/100	6 mos.	Unable to sing or conduct. Climbs one flight slowly.	Rest Nitrites	300 mgm.	Can now sing but cannot conduct. Readily climbs stairs. No nitrites. B.P. 175/90.
2	F	40	C(1)	Pain. Weakness. Dyspnea.	3 mos.	No housework.	Rest	300 mgm.	Able to do housework. Less dyspnea.
3	M	60	H&C(2)	Pain. Dyspnea. B.P. 160/100	10 yrs.	Walks slowly. Pauses on stairs. Lies down after meals.	Rest Digitalis. B-complex Nitrites	250 mgm. Digitalis	Climbs stairs. Works harder. No rest needed after meals. B.P. 140/90.
4	M	52	H	Pain. Dyspnea. B.P. 170/90 Edema plus of the legs. Pulmonary edema.	4 yrs.	Pain when excited. Slow on stairs. Lost his heavy job.		300 mgm.	No pain when excited. Generally improved. B.P. 160/90.
5	M	45	C(1)	Pain. Dyspnea. Weakness.	4 mos.	Slow on stairs. Several attacks per day while selling.	Bed rest	300 mgm.	Cannot run but walks well. Rare pain on considerable exertion.
6	M	67	H&C(1)	Pain. Dyspnea. B.P. 200/100	10 yrs.	Pain when excited. Walks a half a mile.		200 mgm.	No dyspnea nor pain during any farm work. B.P. 170/90.
7	M	61	C(1)	Pain.	2 mos.	Severe pain after walking.		300 mgm.	No symptoms. Smaller Q_2 $S\text{-}T_2$ no longer elevated.
8	F	77	C(1)	Pain. Dyspnea. Auricular fibrillation. Weakness. B.P. 200/100.	6 mos.	Cannot garden.	Digitalis.	300 mgm. Digitalis	Stopped fibrillating. Can garden, previously did not for thirteen years.
9	M	70	H	Pain. Dyspnea. B.P. 190/100	10 yrs.	Pain on climbing steep street. Five to six attacks per day.		200 mgm.	Only one attack in a month on the same routine. B.P. 160/90.
10	M	69		Pain. Dyspnea. Pulmonary edema Bradycardia.	2 mos.	Nocturnal dyspnea. Unable to work.		300 mgm.	Less pain and dyspnea. Only small improvement.
11	M	65		Pain.	1 yr.	Can walk two blocks, slowly. Stops on stairs.		200 mgm.	Can walk farther. Climbs stairs.
12	M	55		Pain. Dyspnea.	2 yrs.	Pain after walking three blocks. Dyspnea on the stairs.		200 mgm.	No improvement.
13	F	62	H	Pain. Dyspnea. Leg edema plus. Pulmonary edema. B.P. 180/100.	3 yrs.	Walks three blocks. Stops on stairs. Needs two pillows.	Rest Digitalis.	300 mgm.	Climbs stairs. Walks farther. No pulmonary edema and leg edema reduced in six weeks. B.P., same.
14	F	63	H	Pain. Dyspnea. Weakness. B.P. 200/105.	1½ yrs.	Excitement.		225 mgm.	Slight improvement. B.P. 200/100.
15	F	66	H&C(1)	Pain. Extrasystoles. Arthritis. B.P. 150/100.	5 yrs.	Unable to climb grades. Occasional pain at rest.	Rest	300 mgm.	Less pain—only slight improvement. B.P. 150/80.

Case	Sex	Age	Etiology	Major signs and symptoms	Duration	Initial tolerance	Previous therapy	Present therapy*	Results
16	M	52	H&C(1)	Pain. B.P. 160/110.	4 yrs.	Walks one and one half blocks. Climbs one flight. Unable to speed lathe.	Rest Nitrites	250 mgm. and 100 mgm. phosphate injectable	No improvement until hypos were begun. Gardens for first time in four years. Walks farther. Works lathe faster. B.P. 145/90.
17	M	45	H&C(3)	Pain. B.P. 140/110.	1 yr.	Unable to swim. Walks three blocks in thirty minutes	Nitrites	300 mgm.	Walks three blocks in eight minutes. Swims fifty yards. B.P. 120/80.
18	M	37	C(1)	Pain. Dyspnea.	6 mos.	Walks six blocks.		200 mgm.	After three weeks could walk twelve blocks.
19	M	54	C(1)	Pain. Dyspnea.	2 mos.	Lost his job. Walks slowly.		200 mgm.	Less dyspnea.
20	M	67	R	Pain. Dyspnea.	6 yrs.	Pain after meals, cold, exertion. Walks one block.	Rest Nitrites (12-15 per day)	300 mgm.	Walks farther and faster. Drove car 2500 miles. No nitrites.
21	M	49	C(1)	Pain. Dyspnea. Enlargement of heart and aortic arch.	2 yrs.	Walks two blocks. Could sit half-day in salesroom.	Rest Nitrites	300 mgm.	Works fulltime as car salesman. Much improved.
22	M	74	H&C(1)	Pain. Dyspnea. B.P. 220/80.	5 yrs.	Walks one block. Stops on stairs.	Rest Nitrites	200 mgm.	Pain gone. B.P. 140/79. Walks fifty percent farther.
23	M	62	C(1)	Pain. Auricular fibrillation. Nocturnal dyspnea. Enlarged heart. Dyspnea. B.P. 210/112.	3 yrs.	Unable to walk.	Rest Digitalis	300 mgm.	Walked one and one half miles on hot day. Still fibrillates. B.P. 130/80.
24	M	69	H	Pain. Edema plus of the feet.	3 yrs.	In bed.		200 mgm.	After fourteen days felt well, gardened. Had silent coronary during treatment, with fair recovery.
25	M	44	C(1)	Pain. Dyspnea.	1 yr.	Climbs one flight slowly. Unable to labor.		300 mgm. hypo of phosphate (300 mgm.)	Laboring. Increased appetite. Still some pain at work.
26	M	66	H&A	Pain. Dyspnea. B.P. 180/90.	6 yrs.	Walks a quarter mile. Unable to hurry on stairs.		200 mgm.	Walks a mile.
27	M	49	H	Pain. Dyspnea. Pulse 120. B.P. 200/140.	2 yrs.	Walks one block.	Rest	300 mgm.	No effect.
								Hypo of 400 mgm. phosphate and 400 mgm., orally	Greatly helped. B.P. 160/90.
28	F	56	H&C(1)	Pain. Dyspnea. B.P. 170/140.	5 yrs.	Some housework. Often forced to lie down.	Phenobarbital	250 mgm.	Can do all but heaviest housework and works all day. B.P. 160/90.
29	M	68	H	Pain. Dyspnea.	8 yrs.	Pain on upgrade near house.	Digitalis	300 mgm.	No pain. Can walk anywhere.
30	M	71	C(1)	Pain. Dyspnea.	10 yrs.	Walks one block. Slow on stairs.		200 mgm.	Normal on stairs. Can walk better. Difficult work untroublesome.
31	M	43	?	Pain. Dyspnea.	2 mos.	One hour of farmwork.		300 mgm.	Does everything on the farm but heavy lifting.
32	M	34	H&C(2)	Pain. Dyspnea. Cyanosis. B.P. 140/110.	2 mos.	In bed.		300 mgm.	Still cyanosed. Back to office work.
33	F	47	H&R	Pain. Dyspnea. Insomnia. Palpitation. B.P. 140/90.	15 yrs.	Light housework, with many rests.		300 mgm.	Less dyspnea. No pain. Full housework. B.P. 130/70.
34	M	66	?	Pain. Insomnia. Leg edema.	4 yrs.	Slow on stairs.		200 mgm.	Well.
35	M	60	C	Pain. Dyspnea. Palpitation.	15 yrs.	Half farm work.		400 mgm.	Harvests wheat all day in the sun. No palpitation.
36	F	55	H	Pain. B.P. 230/95.	6 mos.	Housebound.	Aminophylline Phenobarbital	200 mgm.	B.P. fell to 165/80. Shops. Left bundle branch block unchanged.
37	F	41	H	Pain. Dyspnea. B.P. 220/130.	10 yrs.	Walks two blocks. Light housework.	Nitrites	150 mgm.	B.P. fell to 195/115. Gardens and does full housework.

Case	Sex	Age	Etiology	Major signs and symptoms	Duration	Initial tolerance	Previous therapy	Present therapy*	Results
38	F	47	R	Pain. Occasional ankle edema plus. Dyspnea.	2 yrs.	Light apartment housework.	Digitalis NH_4Cl Salt-free diet	225 mgm.	Swims. Sails, and is active.
39	M	62	H	Pain. Palpitation. Nocturnal dyspnea. B.P. 230/110.	13 yrs.	Walks half block.	Digitalis Aminophylline Phenobarbital	250 mgm.	B.P. 164/88. Does full housework. Rare precordial pain. Began to paint house, but was unable to finish it.
40	M	28	R	Pain. Dyspnea. Ankle edema plus. Pulmonary edema.	1 yr.	Housebound.	Digitalis Aminophylline Phenobarbital	200 mgm.	Now works and can climb stairs at work. Manages apartment. E.K.G.—T_3 became positive in three months.
41	F	52	H	Pain. Nocturnal dyspnea on exertion. B.P. 140/100.	1 yr.	Housework with pain.	Aminophylline Phenobarbital B-complex	200 mgm.	No pain, and can do difficult housework. B.P. 150/90.
42	F	37	R	Pain. Palpitation. Fatigue.	5 yrs.	Light housework.	Aminophylline Phenobarbital	200 mgm.	Can do twice the work formerly done. Now keeping boarders.
43	M	71	C(1)	Pain. Fatigue.	2 yrs.	Walks two blocks.	Aminophylline Phenobarbital	200 mgm.	Drove 4500 miles in past three weeks. Walks ten blocks. Bundle branch block unchanged.
44	M	68	A	Pain. Fatigue. Enlarged heart.	4 mos.	Not working.	Testosterone	250 mgm.	Back to work, driving a bus, No pain.
45	F	52	H	Pain. Marked dyspnea. B.P. 180/90.	3 mos.	Light housework with difficulty.	Aminophylline Phenobarbital Estrogens	200 mgm.	Does full housework without pain. No dyspnea.
46	M	65	C(1)	Pain. Dyspnea. Enlarged heart.	6 mos.	Walks one and one-half blocks. Climbs stairs slowly.	Digitalis	200 mgm.	No dyspnea. No pain. Walks a half mile.
47	M	56	H&C	Pain. Ankle edema plus. Dyspnea. B.P. 210/140.	2 yrs.	Pain while in bed, climbing stairs, or walking a half block.	Aminophylline Phenobarbital	300 mgm.	Two months after his coronary occlusion, walked six miles comfortably. No ankle edema. B.P. 200/130.
48	F	71	H	Pain. Pulmonary edema. Much enlarged heart. Paroxysmal auricular fibrillation. B.P. 190/100.	6 mos.	Light housework.	Digitalis Phenobarbital	200 mgm.	Can do full housework. Very rare fibrillations. Gardens vigorously. No pulmonary edema. No E.K.G. improvement. B.P. 190/92.
49	M	50	C(1)	Pain. Pulmonary edema. Leg edema, three plus.	6 yrs.	Unable to breathe unless sitting in chair. Could not lie in bed. Could not speak complete sentence. Oliguria.	Digitalis Nitrites	400 mgm.	Normal output began in seven days. Returned to work (barber) in three weeks. No edema. Fishing. Plays drums. E.K.G. improved. (S-T recovery).
50	F	29	R	Pain. Markedly enlarged heart. Nocturnal dyspnea. Ankle edema plus Orthopnea.	2 mos.	Light housework.	Digitalis	200 mgm.	Full housework. No edema. No dyspnea.
51	M	53	H	Pain. Severest paroxysmal nocturnal dyspnea. Ankle edema, plus. Moderately enlarged heart. B.P. 270/140.	2 wks.	Marked orthopnea.	Phenobarbital	300 mgm.	Rare, mild nocturnal dyspnea. Sleeps on two pillows. No pain. Drives his car. Unable to work.
52	M	55	H	Pain. Dyspnea. B.P. 190/100.	5 yrs.	Thirty feet of lawn-mowing.	Nitrites	200 mgm.	Mows two lawns. B.P. 150/88.
53	F	50	R	Pain. Dyspnea. Ankle edema, plus. Liver engorgement.	7 mos.	In bed.	Iron Phenobarbital Digitalis	300 mgm.	Becoming ambulant. No symptoms.

Case	Sex	Age	Etiology	Major signs and symptoms	Duration	Initial tolerance	Previous therapy	Present therapy*	Results
54	F	55	H	Pain. Ankle edema, plus. Nocturnal dyspnea.	2 mos.	Marked orthopnea on three pillows. Walks thirty feet.		250 mgm.	No edema. No nocturnal dyspnea. Walks more than a block. "Sleeps all night for first time in twenty years". T_3 now upright in E.K.G.
55	M	76	A	Dyspnea. Moderately enlarged heart. Osteoarthritis. Constant pain.	6 mos.	Idle. Scarcely able to move out of chair.		300 mgm.	Some gardening. Less dyspnea. Occasional dull ache in chest. Arthritis, slightly improved.
56	M	48	C(1)	Nocturnal pain. Slight enlargement of heart.	1 yr.	Walks two blocks.		200 mgm.	Walks one mile. Still slight pain on moderate work. No nocturnal pain.
57	M	69	H&C(1)	Pain. Pulmonary congestion. Dyspnea. B.P. 150/108.	4 yrs.	Unable to walk ten feet.	Phenobarbital	250 mgm.	After eight days treatment, complete relief of pain for three days. Died suddenly one week later.
58	F	74	A	Pain. Dyspnea. Recent ankle edema, plus.	6 mos.	Not compensated at bed rest.	Digitalis	250 mgm.	Up and about apartment. No edema. No dyspnea.
59	F	67	H&C(1)	Pain. Dyspnea. Ankle edema, plus. B.P. 210/100.	2 mos.	In bed.		200 mgm.	B.P. 180/90. Occasional pain. No edema. No dyspnea. Light housework.
60	M	54	H&C(1)	Pain. B.P. 210/110.	3 yrs.	Walks three blocks. Firing the furnace causes pain. Unable to work. (traveller)	Nitrites	175 mgm.	Able to work. Estimates his pain decreased eighty percent. B.P. 174/98.
61	M	54	A&C(1)	Pain. Dyspnea. Ankle edema plus.	4 yrs.	Retired. Unable to do household jobs.	Aminophylline Phenobarbital	250 mgm.	Mows lawn. Occasional discomfort.
62	M	40	R	Pain. Dyspnea. Ankle edema plus. Marked heart enlargement. Complete block. B.P. 162/10.	9 yrs.	Idle. Could not deliver gas at service station.	Digitalis	200 mgm.	B.P. 172/52. Regular rhythm. Carried cement blocks four hours before pain recurred.
63	M	29	R	Pain. Dyspnea. Ankle edema plus.	2 yrs.	Walks one block. Intermittently confined to bed.	Phenobarbital Digitalis Nitrites (10 tabs. per week)	200 mgm.	Works (chartered accountant). Walks four blocks. No nitrites.
64	F	73	A	Pain. Dyspnea. Ankle edema plus. Slight liver enlargement. Auricular fibrillation. B.P. 180/120.	7 yrs.	Unable to walk thirty feet.		300 mgm.	B.P. 160/100. Walks three blocks. Unable to wear any of her old shoes — all too large. Still fibrillates.
65	M	54	C(2)	Pain. Dyspnea.	7 yrs.	Fifteen Masters trips raised B.P. 24 mm. Hg. and pulse 44 beats per minute. Continual pain.	Prophenamine	250 mgm.	Sixteen trips raised B.P. 6 mm. Hg. and pulse 4 beats per minute. Pain disappears three to four days at a time, and then very mild.
66	F	72	H&C(1)	Pain. Dyspnea. Ankle edema plus. Ascites. Pulmonary edema. Marked enlargement of heart. B.P. 290/110.	3 yrs.	Progressive failure.	Nitrites Digitalis	400 mgm.	No congestive failure. B.P. 200/120. Able to cook.
67	F	55	H	Pain. Arthritis. Slight enlargement of heart. Nocturnal dyspnea. B.P. 200/100.	1½ yrs.	Unable to walk one block.	Digitalis	250 mgm.	Does full housework. Milks two cows. Can walk over three blocks. No nocturnal dyspnea. B.P. 190/100.
68	M	69	C(1)	Pain.	9 mos.	Unable to walk ten feet.	Aminophylline Codeine	300 mgm.	No help.
								325 mgm.	Slight help.
								350 mgm.	Idle in and out of the house.

Case	Sex	Age	Etiology	Major signs and symptoms	Duration	Initial tolerance	Previous therapy	Present therapy*	Results
69	M	65	R.H. C(1)	Pain. B.P. 206/115. Dyspnea.	14 yrs.	In bed.		250 mgm.	Can work, with occasional mild pain. B.P. 180/110.
70	F	67	H	Pain. Dyspnea. B.P. 300/130.	1 yr.	Could not reach or lift. Could not walk one block.	Digitalis Phenobarbital	300 mgm.	Full housework. Walks four blocks.
71	F	58	H	Pain. Complete right hemiplegia one and one-half yrs. ago. B.P. 250/120.	10 yrs.	Assisted about the house because of palsy—this elicited pain.	Digitalis	300 mgm.	Can walk one and one-half blocks slowly, without pain. Can sew with right arm and talk clearly.
72	M	40	C(1)	Pain. Dyspnea.	9 yrs.	Light work. (foreman)	Aminophylline	300 mgm.	Works hard thirteen hours per day.
73	F	45	R	Pain. Dyspnea. Auricular fibrillation. Ankle edema plus.	2 yrs.	Light housework. Pain every day.	Digitalis	400 mgm.	Still fibrillating. Full housework. No pain.
74	M	42	H	Pain. A-V block. Ankle edema plus. B.P. 188/108.	10 yrs.	Idle.	Digitalis	600 mgm.	B.P. 160/120. No improvement. Blood cholestrol fell from 383 mgm. percent to 225 mgm.
75	F	68	A.R.	Pain. Dyspnea. Ankle edema plus.	12 yrs.	Walks two blocks. Needs two pillows.	Digitalis	300 mgm.	Shops four blocks away from home. Ankle edema disappeared. One pillow.
76	M	42	R&C(3)	Pain.	3 yrs.	Walks a half block. Five Masters trips raised B.P. 12 mm. Hg. and did not accelerate pulse.	Phenobarbital	300 mgm.	Walks two blocks. Eleven Masters trips raised B.P. by 16 mm. Hg. and did not accelerate pulse.
77	M	68	A	Pain. Dyspnea.	6 yrs.	Unable to hurry. Eight Masters trips lowered B.P. 10 mm. Hg. and raised pulse 4 beats per min.	Nitrites	300 mgm.	Drove his car all night by himself. Needs less than half as much nitrites. No edema. No liver enlargement.
78	F	61	H	Pain. Dyspnea. Ascites. Ankle edema plus. Extrasystoles. B.P. 184/110.	10 yrs.	Idle.	Estrogen	250 mgm.	No extrasystoles. Light housework. No edema. B.P. 194/104.
79	M	42	R.H.	Pain. Fibrillating. Pulmonary edema. Dyspnea. B.P. 170/95.	9 yrs.	Nursed four hours per day despite great pain. Three pillows. Walks thirty feet. Up two hours each night.	Digitalis	250 mgm. Phenobarbital Aminophylline Digitalis	B.P. 166/98. Still fibrillating. Still nurses four hours per day, with less pain. Walks three blocks. Rare nocturnal dyspnea. Sleeps all night.
80	F	60	C(3)	Pain. Dyspnea. Ankle edema plus. B.P. 160/100.	11 yrs.	Can walk less than a block or one flight of stairs.	Nitrites	300 mgm.	B.P. 160/100. Walks three blocks. Not much improved. No nitrites needed.
81	F	68	A	Pain. Pulmonary edema. Ankle edema plus.	6 wks.	Walks one block slowly.	Digitalis Aminophylline Nitrites	200 mgm.	No nitrites. No edema. Packed household effects for three days with no pain.
82	M	67	C(1)	Pain. Nocturnal dyspnea. Ankle edema plus.	1½ yrs.	Walks less than one block. Sat in the store all day long.	Nitrites Mercurials	250 mgm.	Works actively all day as a store clerk. No dyspnea. No edema. No nitrites.
83	M	67	A	Pain. Dyspnea. Enlarged heart.	3 yrs.	Walks less than one block. Three pillows.	Digitalis	300 mgm.	Walks all over the village readily. One pillow.
84	M	43	R	Pain. Dyspnea. Weakness. Enlarged heart. Mottled legs.	2 yrs.	Walks fifty yards. Three pillows.	Digitalis	250 mgm. 350 mgm.	No help. Mottled color of legs fading. "Walks to back of farm and picks berries all day." One pillow.

LEGEND

M—Male
F—Female
H—Hypertension

C—Coronary disease
R—Rheumatic disease
A—Arteriosclerosis

C(1)—One coronary attack
C(2)—Two coronary attacks
C(3)—Three coronary attacks

*In this and in subsequent papers, an attempt has been made to express the dosage of vitamin E in terms of alpha-tocopherol. This is designed to facilitate clinical comparison between different preparations now on the market, since dosage is of fundamental importance in our treatment. Accordingly, any capsule containing "50 mgm. of natural mixed tocopherols" has been crudely equated to 25 mgm. of alpha-tocopherol. The only exception has been in the case of phytoferol, where the pharmaceutical house does this.

Perusal of the above case histories will demonstrate that the great majority showed definite signs and symptoms of heart disease other than precordial pain. These were all instances of an organic disease as far as could be ascertained by clinical, electrocardiographic and roentgenological studies. No patients who sought relief have been refused, however desperate their condition. More recent experience has suggested the value of larger doses of vitamin E than that used in many of the first cases. This increased dose and longer observation would probably improve the figures here presented.

Summary

This study led us to the conclusion that vitamin E in large doses is of value in the treatment of anginal pain.

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†Second of a series of five papers.

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They also wish to emphasize the role Mr. Floyd R. Skelton has played in these purpura-heart researches. It would be hard to exaggerate his contribution.

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Vitamin K In Spinal Anesthesia With Procaine*

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In a previous paper (1), the effects of anesthesia on the prothrombin level of the blood were reported. It was concluded that "ether anesthesia shortens the prothrombin time markedly, while spinal anesthesia with procaine does not seem to have any influence upon the prothrombin time". In fact, it was found that during spinal anesthesia with procaine, the prothrombin time was somewhat lengthened, which was contributed to the preoperative sedation the patients in this group received. On the other hand, ether anesthesia not only neutralized this lengthening effect, but also markedly decreased the prothrombin time of the blood. Thus a correlation was made between the results of this study and the possible incidence of postoperative emboli in the ether group, and the possibility of postoperative hemorrhage in the spinal group. It was also stated in this paper that on the basis of a somewhat superficial, preliminary study, the administration of vitamin K, before and during anesthesia, seemed to be of benefit in the latter group.

For this reason, a more elaborate, separate study was undertaken upon a group of patients who underwent spinal anesthesia with procaine. This study dealt specifically with the effect of vitamin K upon the prothrombin time of the blood, and its possible prophylactic value in the prevention of postoperative hemorrhage.

The results of this research are herewith reported.

Material And Methods

The group for the present study consisted of seventy-five patients between the ages of twenty-seven and sixty-eight years. Males and females were about equally represented. The studies were carried out upon a great variety of operative cases, including simple dilatations and curettages, hemorrhoidectomies and cystoscopies; as well as gastrectomies, cholecystectomies and difficult laparotomies. The amount of procaine used as the anesthetic, naturally varied with the type and expected length of the operation, but it usually ranged between 50 and 200 milligrams. No cases receiving continuous spinal anesthesia were included in this study.

The methods used here were the same as those employed in the previous study (1). The prothrombin time was determined with the "Bedside method" of Smith *et al.* (2). The thromboplastin solution was prepared from a crude lung extract.[1] The average, normal prothrombin time, as determined from the blood of normal controls, was 27.9 seconds, which represents 100 percent in the Smith test. In the remainder of this paper the terms "prothrombin time" and "clotting power" are used interchangeably —a high prothrombin time denoting a low clotting power and vice versa.

Five prothrombin time determinations were done on each patient. The first test was performed shortly after the patient was admitted to the hospital and before he had received any medication. The second test was done before the start of the anesthesia, i.e., after the patient had had the full effect of the preoperative sedation. This consisted of sodium pentobarbital, grains III, both the night before and early the morning before the operation; also additional morphine sulfate, grains 1/4, and scopolamine, grains 1/100, before going to the operating room. The prothrombin time was tested for the third time when the patient had shown the full benefit of the spinal anesthetic, i.e., usually about fifteen to twenty minutes after the anesthetic was given, at a time when the desired anesthesia level was reached. The test was performed for the fourth time approximately six hours after the end of the operation, and for the

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[1]Both the thromboplastin solution and the vitamin K preparation (Synkamin) used in this study, were kindly supplied by the Parke, Davis & Company.

fifth and last time, twenty-four hours later, at a time when the anesthetic had completely worn off.

The seventy-five patients of this study were divided into three groups (A, B and C) consisting of twenty-five patients each. This was done according to the time that the patients received vitamin K. Group A received vitamin K immediately after the second prothrombin time determination was done, i.e., just before the anesthetic was given. Group B had vitamin K administered immediately after the third prothrombin time determination, i.e., about twenty minutes after the anesthetic was given and at a time when the operation was in full progress. Group C did not receive vitamin K at all and thus served as controls. The patients who received vitamin K were all given the same dosage, namely 2 mg. of Synkamin intravenously, regardless of what their individual prothrombin time was.

Results

As pointed out previously, the normal prothrombin time with the Smith Bedside Test, as employed in this study, was 27.9 seconds which is considered 100 percent.

For the first time the prothrombin time was taken shortly after the patients had entered the hospital and before they had received any medication. The average prothrombin time in the entire group of seventy-five patients was 27.9 seconds, or 100 percent of normal as expressed by the Smith test. In each of the three subgroups (A, B and C) the average prothrombin time was also 27.9 seconds or 100 percent of normal.

After the patients received the full benefit of the preoperative sedation, the prothrombin time was taken for the second time; this was done shortly before the anesthetic was given. At that time, the average prothrombin time in the entire group was 31.2 seconds, or a little over three seconds longer than on the first test. This represented 89.4 percent of the normal clotting power as interpreted by the Smith test. The same average prothrombin time of 31.2 seconds or a clotting power of 89.4 percent was also found in each of the three subgroups. Following this second test, each of the twenty-five patients in group A received 2 mg. of vitamin K (Synkamin) intravenously.

The tests were performed for the third time when the desired level of anesthesia was reached, approximately twenty minutes after the anesthetic was given and at a time when the operation was in full progress. The average prothrombin time in the entire group was 29.0 seconds or the clotting power was 96.7 percent of the normal. When these figures are broken down into the three different groups, they at once become more striking. Group A, the group which received vitamin K, showed an average prothrombin time of 25.9 seconds or a clotting power of 107.7 percent of normal, while both group B and C, the groups which did not receive vitamin K, showed an average prothrombin time of 30.6 seconds or a clotting power of 91.2 percent of normal. Thus, the twenty-five patients receiving vitamin K showed an average decrease of prothrombin time of almost five seconds (meaning an increase of 16.5 percent in the clotting power of the blood), as compared to the patients who were not given vitamin K. After the third prothrombin time determination was made, each of the twenty-five patients in group B received 2 mg. of vitamin K (Synkamin) intravenously.

Six hours after the end of the operation, the prothrombin time was taken for the fourth time. At that time, the average values in the entire group of seventy-five patients were 27.3 seconds, or 102.6 percent of the normal clotting power as interpreted by the Smith test. Broken down into the three separate groups, group A showed an average prothrombin time of 25.7 seconds (or a clotting power of 108.6 percent); group B, an average prothrombin time of 26.5 seconds (or a clotting power of 105.3 percent), and group C, the group which did not receive vitamin K, an average prothrombin time of 29.7 seconds (or a clotting power of 94 percent of normal). Here again the group which received vitamin K (group B) showed an average decrease in the prothrombin time of almost four seconds (or an increase of 14.1 percent in the clotting power of the blood), while the group which did not receive vitamin K (group C) showed a decrease of only 0.9 seconds, or an increase of 2.8 percent in the clotting power of the blood.

The test was performed for the fifth and last time, twenty-four hours after the fourth determination at a time when the anesthetic had completely worn off, but when the patients were receiving the greatest amount of postoperative analgesics and sedations. The results were approximately the same as those of the fourth test. The average prothrombin time in the entire group of seventy-five patients, was 27.4 seconds, meaning a clotting power of 102.3 percent of normal. Group A showed an average prothrombin time of 25.9 seconds (or a clotting power of 107.7 percent of normal); group B an average prothrombin time of 26.5 seconds (or a clotting power of 105.3 percent of normal), and group C an average prothrombin time of 29.7 seconds (or a clotting power of 94 percent of normal).

The entire results are shown in Table I and Chart I.

	GROUPS			
TEST	A	B	C	ENTIRE
I	27.9	27.9	27.9	27.9
II	31.2	31.2	31.2	31.2
III	25.9	30.6	30.6	29.0
IV	25.7	26.5	29.7	27.3
V	25.9	26.5	29.7	27.4

Table I: Average Prothrombin Time, in Seconds, of the Five Tests in the Different Groups of Patients (see text).

Discussion

The administration of vitamin K, and procaine before or during spinal anesthesia, seems to be of definite benefit. It not only causes a definite increase in the clotting power of the blood, which is lowered

under the spinal anesthesia with procaine, as a result of the preoperative sedation, but it also seems to be of a prophylactic value in the prevention of postoperative oozing. This statement is based on the results of the present study, in which a total of seventy-five patients who received spinal anesthesia with procaine were examined, and during which time, five separate prothrombin time determinations were performed on each patient. Fifty of the seventy-five patients received vitamin K—twenty-five before the start of the anesthesia, and twenty-five under anesthesia—while twenty-five patients did not receive any vitamin K at all and thus served as controls.

In analyzing the results of this study, it will be seen that following the administration of the preoperative sedation, a definite lowering of the prothrombin time took place in the entire group. It has been repeatedly reported that sodium pentobarbital, which was used as the main preoperative sedation in this study, caused a definite lowering in the prothrombin time of the blood (1,3,4), and it seems to be a generally accepted fact. The average prothrombin time of the entire group of seventy-five patients following preoperative sedation, was almost 3.5 seconds longer than the admission values. When vitamin K was given to one group of patients (group A), there was a definite increase in the clotting power of the blood in this group (from 89.4 percent

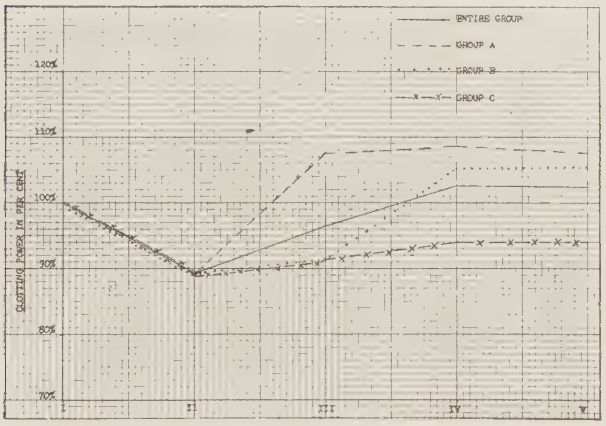

CHART I

to 107.7 percent), while the other two groups which did not receive vitamin K at all, showed only a minimal increase in the clotting power of the blood (from 89.4 percent to 91.2 percent). This minimal increase might be explained, in view of the fact that the preoperative sedation which caused a lowering of the prothrombin time, might have partly worn off at the time the tests were performed (1). The definite increase in the clotting power of the blood of those in group A, was still evident during the fourth and fifth tests, which were performed six, and thirty hours respectively, after the end of the operation. This probably indicated that once the "lengthening" effect of the preoperative sedation is overcome and the prothrombin time restored to normal, it will remain at a normal level. This same phenomenon could be observed in group B, which received vitamin K during the height of the operation. While up to this point in group B, the clotting power of the blood was below normal (91.2 percent), following the administration of vitamin K, it improved by more than 14 percent (to 105.3 percent) and was still at the same level at the time of the fifth test. On the other hand, group C which did not receive vitamin K either before or during anesthesia, showed only a minimal improvement in the clotting power of the blood, without ever reaching the "normal" values. Thus, while the average clotting power of group C in the fourth and fifth tests was only 94 percent of normal, the average clotting power for group B on the same two tests, was 105.3 percent and for group A, 108.6 percent and 107.7 percent, respectively. This means that there was an average increase in the clotting power of the blood in group A of over 14 percent, and in group B of over 11 percent, as a result of the action of vitamin K given to both these groups.

Very interesting in this connection are the comments of the surgeons who performed the various operations. Before elaborating on these, it should be mentioned that their opinions were in no way biased or prejudicial. None of the quoted surgeons was even aware of the fact that his patient had received vitamin K, or when he had received it. The patients comprising group A received their vitamin K while still in the anesthesia room, while those of group B received their vitamin K immediately following the withdrawal of blood for the prothrombin time determination, and the surgeon was unaware of the switch of syringes which took place underneath the drapings. The same procedure was also carried out in group A and group C when the blood was taken for the prothrombin time determinations. Group C did not receive vitamin K at all.

In all but two of the cases in group A, the surgeons commented that the "operative field" was cleaner than usual, since there was not as much oozing and hemorrhage, which if it did occur, was easily controlled. In none of the cases did postoperative oozing through the incision occur.

Similar comment was heard about the patients of group B with the exception of the comment about the operative field. Here too, there was no postoperative oozing through the incision in the entire group.

No unusual comments were heard about the patients of group C. The operative field was about the same as usual and postoperative oozing through the incision occurred with the same average frequency.

Summary And Conclusion

1. The effect of vitamin K upon the prothrombin level of the blood, given to patients while under spinal anesthesia with procaine, is discussed.

2. A total of seventy-five patients, fifty of whom received vitamin K, either before or during anesthesia, and twenty-five of whom did not receive vitamin K, thus serving as controls, were studied.

The prothrombin time determinations with the Smith Bedside Test were performed five times on each patient. The determinations were done for the first time shortly after the patient's admission to the hospital, for the second time after the patient had received the full benefit of the preoperative sedation, for the third time when the desired level of the anesthesia was reached and when the operation was in full progress, for the fourth time six hours after the end of the operation, and for the fifth and last time twenty-four hours later.

3. The results of this study clearly show that the administration of vitamin K, before or during spinal anesthesia with procaine, seems to be of definite benefit. It causes a definite increase in the clotting power of the blood which is lowered under spinal anesthesia with procaine, due to the preoperative sedation, and it also seems to be of prophylactic value in the prevention of postoperative oozing.

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Surgery of Thyrotoxic Goiter

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Patients affected with thyrotoxic goiter often improve to such a degree with the treatment of thiouracil, that an operation may sometimes be unnecessary. At times, x ray therapy or the administration of Lugol's iodine solution may also result in improvement. The results of these treatments are, a reduction of the metabolism rate, a remission of symptoms and a gain in weight. When the improvement becomes permanent, the patients who have been treated in this fashion may never have recourse to surgery; however, when it is found that an operation is required, the treatments that the patient has undergone, which may occasionally prove curative, cannot always be considered a good preparation for surgery.

All these improvements represent changes in the general condition of the patient, however there also occurs other important changes that affect the anatomical structure of the layers of muscles and fascias covering the thyroid itself. These changes are not visible and are not recognizable at the external examination of the patient, but are discovered only during the operation. They render the operation more laborious and difficult, since these layers serve as a necessary guide in the various steps of the operation—and when not perfectly normal can mislead the surgeon. It is obvious that the difficulties met with in performing a thyroidectomy are in direct relation to the number and extension of the changes of these tissues. At best, thyroidectomy is a difficult operation, requiring a perfect knowledge of the anatomy of the neck, and many times over-taxing the ability of expert surgeons. Difficulties increase in direct proportion to the number and extension of changes of the different elements of the cervical region.

In years past, when the preparation for surgery that is now considered indispensable was not thought necessary, and goiter patients were operated on without any previous medical preparation, thyroidectomy usually was a perfect anatomical operation. All the strata of the cervical region were clearly defined, easily separated and evident. After the skin was incised, the platysma myoides, the superficial and middle fascias, the sterno-hyoid and the sterno-thyroid muscles were clearly exposed in succession; it was not difficult to separate or incise them and make the capsule evident. Generally afterwards, the thyroid was easily mobilized. The operation was performed with almost the same security as an anatomical preparation performed in the dissecting room.

Of course a great improvement in the performance of the operation was due to the adoption of the transversal incision of the skin, but even in the epoch when following the advice of Bottini, the operation was performed with a middle vertical incision of the skin, the operation was not very difficult and was relatively safe. This is also the case when no preparation is made before a thyroidectomy or when Lugol's solution is used, but in the author's experience, the case is quite different when the other preparations are used. Since most patients with a goiter have been medically treated before being referred to the surgeon, it is important to know what kind of treatment was used.

Of the patients that have come to the author for a goiter operation, some have already been treated with x rays, many with the administration of Lugol's solution and more recently, a few patients have been treated with thiouracil. When a goiter has previously been treated with x rays, the operation is difficult and quite different from an operation on a patient that had not received any medical preparation or had been treated with Lugol's solution. In operating after the x ray treatment, it is not always

possible to distinguish the muscular structure of the platysma myoides or to separate the various aponeuroses. Instead of being clearly exposed, it seems that all the anatomical layers are blurred and have the appearance of being atrophic, indurated and almost fused together, nor is it easy to separate the sternal muscles and expose the capsule. There is also a great deal of bleeding and the thyroid is friable and easily lacerated.

More recently, in cases where thiouracil has been used, the writer found that the operation was an arduous undertaking, and that the same conditions and the same difficulties were present as in the cases where x ray treatment had been previously administered. The author cannot help feeling that the operation would have been easier and more successful if thiouracil had not been administered before the operation.

Summary

In conclusion, the author wishes to state that he does not believe that x ray treatment should be administered before a surgical operation of the thyroid; that the use of thiouracil for a thyroidectomy needs more study, and that at the present time, it should not be adopted as a standard preparation for an operation in all cases of goiter. He believes that at present, the use of Lugol's solution before the operation is satisfactory, and it should be considered sufficient until another and better way is found that will not only improve the general condition of the patient, but will have no action or influence on changing or altering the anatomical structure and appearance of the layers of tissue covering the thyroid layers; since these tissues need to be incised and dissected before the thyroid can be excised.

43 West Eleventh Street.

Evaluation of a New Hypotensive Formula*

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Although a number of drugs in the nitrite group have been widely employed for many years in the treatment of essential hypertension, today many authorities incline toward the view that only those which exert a comparatively prolonged effect provide a rational therapeutic approach to the problems presented by the patient with high blood pressure. Boyer (1), for example, states that drugs which produce a sudden, brief fall in blood pressure are not only without value in controlling the hypertensive state, but that their use is not entirely free from danger.

According to Goodman and Gilman (2), mannitol hexanitrate exerts a more sustained hypotensive effect than any of the other nitrites commonly employed. The term "nitrite" is here used to include both nitrites and nitrates, since the latter depend upon the liberation of the nitrite ion in the body for their action. Following the administration of mannitol hexanitrate, the fall in blood pressure begins in approximately fifteen to thirty minutes and lasts from four to six hours.

Weaver and his associates (3), made a careful comparative study of the four nitrite drugs most widely used in the treatment of hypertension: nitroglycerin, sodium nitrite, erythrol tetranitrate and mannitol hexanitrate. Their results in general confirmed the figures given by Goodman and Gilman, although they found that the duration of the effect of erythrol tetranitrate and mannitol hexanitrate was approximately the same. However, a larger percentage of subjects responded to mannitol hexanitrate than to erythrol tetranitrate.

The incidence of untoward reactions was also studied by these workers and was found to be lower with hexanitrate of mannitol than with any of the other drugs used. Following a single dose, disagreeable side effects were noted in ten of the thirty-two subjects given nitroglycerin, in two of the twenty-eight receiving sodium nitrite, and in four of the twenty-four after erythrol tetranitrate. Of the twenty-eight persons who were given a single dose of mannitol hexanitrate, none showed any ill effects. Nevertheless, under continued administration, eight of the fifteen patients receiving mannitol hexanitrate developed undesirable reactions such as headache, dizziness or gastrointestinal symptoms. In two instances these reactions were slight and transitory, but in six cases they were of sufficient severity to lead to a discontinuance of therapy. In those patients who tolerated the drug well, the relief afforded from the symptoms of hypertension was often striking.

Another drug which, according to numerous published reports, has afforded symptomatic relief in a large percentage of hypertensive patients is viscum album, the European mistletoe.

Among the more recent studies of viscum album is that of Boyd and Weissberg (4), who administered the drug to forty hypertensive patients, all of whom presented cerebral symptoms such as headache, dizziness and tinnitus. An amelioration of symptoms ranging from slight to complete was observed in twenty-nine instances (72.5 percent). Reduction in the blood pressure was less frequent; a definite fall was noted, however, in seventeen cases (42.5 percent). Symptomatic improvement was observed even in patients with malignant hypertension whose blood pressure continued to rise during the period of observation. No evidence of intolerance to viscum album was noted. Boyd and Weissberg stress the fact that the clinical use of the drug

*This investigation was aided by a research grant from the Anglo-French Laboratories, Inc., New York, N.Y.

is attended by no danger of toxic effects. In an extensive review of the literature, they found a remarkable unanimity of opinion on this point, as well as on the effectiveness of viscum album in the relief of the subjective symptoms of hypertension.

As it is generally recognized that blood pressure may be affected by the mental and emotional state of the patient, the work of Baldauf (5), is of particular interest. It was he who employed viscum album for the treatment of the hypertensive state in psychotic patients. His subjects included a number of persons with dementia praecox, who showed the indifference to environment characteristic of that condition. In some of these cases there was a reduction in the blood pressure of as much as 30 or 40 mm. of mercury; a result which, in Baldauf's opinion, eliminated the possibility of a purely suggestive influence. Excellent results were also obtained in the relief of the cerebral symptoms.

Good results with viscum album in the management of hypertension with associated arteriosclerosis have been reported by various authors. Danzer (6), found the drug useful in a number of cases of this type which had proved refractory to other methods of treatment. Coruzzi (7), administered viscum album to twenty-five hypertensive patients, all of whom had definite signs of arteriosclerosis. In most cases there was notable symptomatic relief throughout the period of observation (from one to two months) and in some instances there was a reduction in blood pressure of from 30 to 40 mm. of mercury, which was well sustained.

In view of the reactions which sometimes accompany the continued administration of mannitol hexanitrate, especially when larger doses are employed, it appeared that if its action could be reinforced by a synergistic combination with a drug which was completely nontoxic in therapeutic dosage and which had proved effective in relieving the symptoms of high blood pressure, a preparation might be obtained which would approach more closely the ideal requirements for hypotensive therapy. A minimal dosage of mannitol hexanitrate might thus be made effective with a consequent avoidance of side effects, while the efficiency of the nitrite in controlling subjective symptoms would be augmented. Viscum album appeared to meet the criteria for the desired synergistic agent.

Plan of Investigation

In order to determine the efficacy of such a synergistic combination, pharmacologic and clinical studies were carried out, using the following formula*: Hexanitrate of mannitol 8 mg. (diluted with 9 or more parts of lactose to make it nonexplosive), solid extract viscum album (4:1) 50 mg. with excipients and coating.

The investigation was carried out in three parts: 1. a clinical study to determine the duration and average extent of the action of the hypotensive formula employed; 2. a comparison of the total average effect of the compound on human subjects with that of a placebo; and 3. a determination of the pharmacodynamic action of the formula on animals.

*Available for prescription as Hepvisc Tablets.

First Clinical Study

Ten patients with arterial hypertension were selected for this phase of the investigation. There were five females and five males in the group. The ages of the patients ranged from twenty-three to sixty-two years, and the initial systolic blood pressure reading from 160 mm. to 260 mm. of mercury. The urea nitrogen determinations ruled out kidney complications in all cases.

Procedure:—After the patient had rested quietly for half an hour, three blood pressure readings were made and the average was accepted as the initial pressure. Two tablets of the hypotensive compound were then administered and blood pressure readings were made thereafter at the end of the first, second, third and fourth hours. The blood pressure was measured in every instance by the mercury sphygmomanometer, and palpation was used as a check on the auscultatory readings. The pressure in the cuff was quickly increased in steps of 10 mm. of mercury, until the radial pulse disappeared, after which it was allowed to fall rapidly. If the radial pulse returned to a higher level than that at which the first sound was heard, the palpatory reading was accepted as the systolic pressure; otherwise the auscultatory reading was accepted.

Results:—Of the ten patients, eight showed a fall in blood pressure, as a result of a single dose of two tablets of Hepvisc. As a rule, the greatest decline occurred during the first hour, although in some instances the downward trend continued through the second hour. After reaching the lowest reading, the return to the original figure was gradual, the hypotensive effect being prolonged in most cases through the third or fourth hour after administration. The greatest total reduction in systolic blood pressure was 30 mm. of mercury; the greatest fall in diastolic pressure was 10 mm. The average reduction in systolic pressure for the entire group, including the two patients who failed to respond to medication, was 9.8 mm. When the figures representing changes in both systolic and diastolic pressure were combined to obtain a total index of change, the average fall was 9.2.

Second Clinical Study

In this part of the investigation, the changes in blood pressure produced by a single dose of Hepvisc were compared with those following the administration of a placebo. The placebo was given in the form of a tablet similar in appearance to the Hepvisc tablet but without pharmacodynamic effect. The subjects included eight males and fourteen females, all of whom were suffering from arterial hypertension. The ages of the patients ranged from thirty-five to seventy years. Kidney disease was ruled out in every case.

Procedure:—The procedure was the same as that used in the previous study, except that in this series the Automatic Tycos Recording Sphygmomanometer

was used. This instrument makes an objective record, with an inked line, of the diastolic and systolic blood pressure and the pulse pressure. In cases where the pulse pressure was extremely low as a result of myocardial damage, it was impossible to get good tracings. In these cases, therefore, it was necessary to measure the blood pressure by the auscultatory method with the mercury sphygmomanometer.

Results:—The results in those cases in which a clear recording was obtained by means of the Automatic Tycos Recording Sphygmomanometer were tabulated. The blood pressure changes following the administration of a placebo and those following a single dose of the hypotensive compound were recorded and compared. Where both a rise and a fall in blood pressure occurred, the result was given as the algebraic sum of the greatest plus and minus change, thus providing as accurate an indication of the effect as possible. The index of the total change for the entire group was arrived at by obtaining the algebraic sum of the average change in the systolic and diastolic pressure.

The average change following the administration of a placebo was a rise of 4.4 mm. in the systolic pressure and a fall of 4.2 mm. in the diastolic, giving an index of total change of plus 0.2. After a single dose of the hypotensive compound, on the other hand, the average change was a fall of 11 mm. in the systolic pressure and a fall of 5.45 mm. in the diastolic; giving an index of change of minus 16.45. It is obvious that this constitutes a statistically significant difference.

Similar results were obtained when the mercury sphygmomanometer was used. After administration of the placebo, there was an average rise of 2.08 mm. in the systolic and of 0.92 mm. in the diastolic pressure. Thus, the total index of change was plus 3.0. In contrast, when a single dose of Hepvisc was given, there was an average reduction of 9.4 mm. in the systolic and of 1.3 mm. in the diastolic pressure. This is a total index of change following the administration of the hypotensive compound of minus 10.7.

Animal Studies

Since cats have a blood pressure which is nearly the same as that of human beings and since they are easily obtainable, they were selected for this experiment.

Technique:—After the animals had been lightly anesthetized with ether, an incision was made high and to the right of the breast-line, to expose the carotid artery. The carotid artery was separated from the nerve and a cannula was inserted and tied into place. This cannula was connected to a line containing a saturated sodium bicarbonate solution which was attached to a pressure reservoir. In addition, a continuous connection was made with a blood pressure recording machine which ran at a constant speed, on which notations were made from the mercury blood pressure reading machine.

Procedure:—A number of animals were run on anesthesia alone, in order to provide a control group. The remainder of the animals received the medication by the intraperitoneal route after the blood pressure was stabilized. The initial blood pressure of the animals was recorded at an average of seven readings taken at five minute intervals. After the injection, readings were taken at twenty minute intervals for three hours.

Medication Used:—Hepvisc was finely ground in a mortar and diluted to form a solution containing 100 mg. of the drug per cubic centimeter. The dosage used was 100 mg. of the hypotensive compound per kilogram of body weight.

Results:—In estimating the results, if both a rise and fall of the blood pressure occurred, the effect was considered to be the algebraic sum of the greatest positive and negative change. The average fall in blood pressure for the group of animals on ether anesthesia alone was 10.6 mm. The maximum fall in this group was 15 mm. In the group of cats receiving Hepvisc, the average reduction in blood pressure was 35.1 mm. The maximum reduction was 70 mm. Thus Hepvisc, when administered to cats, appeared to produce a striking fall in blood pressure, as compared with the ether anesthesia alone.

Summary

In each of the studies described, the hypotensive formula under investigation produced reductions in blood pressure of statistical significance. The total indices of change in the three studies on hypertensive human subjects were, respectively, minus 9.2, minus 16.45, and minus 10.7. In the animal studies, the index of change was minus 35.1. It appears that hexanitrate of mannitol in combination with viscum album is pharmacologically and clinically effective in reducing blood pressure.

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Samuel Wilkes, born in England in 1824, described a disease produced by post mortem examination which we know as *Wilkes' disease,* or verruca necrogenica. Darier notes that the disease was described by Laennec. Wilkes died in 1911.

Editorials

The Fight Against the Antivivisectionists

The city of Chicago has the undeserved distinction of being the headquarters of the group, which for many years has fought against animal experimentation on the grounds that experimenters are barbarously cruel and that their work is unnecessary and nonproductive of any good result. A few months ago, we referred editorially to advertisements which appeared in the metropolitan newspapers and which emanated from the same Chicago headquarters, condemning laboratory experiments upon animals, and asking for public support to be directed against the practice. It is just as well to recognize at once, that these socalled "crackpots" are to be reckoned with as redoubtable foes. They are voluble, vocal, energetic, constant and indefatigable in their misplaced zeal for their cause. It is a sort of fanaticism which gathers speed and power as it rolls on. Therefore, every physician, clinician, researcher, diagnostician or specialist in any small corner of the field of medicine, must keep informed of what is going on and provide himself with the facts, as well as the fancies. He will need to know how to combat wild and untruthful statements with truthful and well-balanced arguments.

It so happens that the *Roche Review*, December, 1946, carried a twelve-page, unsigned, informative article entitled "More Dogs or Better Babies?" The subtitle states that it is a survey of the current status of animal experimentation. It is, indeed, a thoroughly commendable resumé of the situation, pro and con to date, and should be read by everyone who is at all interested in public or private health problems; and who is not so interested?

In Chicago during 1944 and 1945, the antivivisectionists (this is their own self-styled title) under the leadership of Mrs. Irene Castle McLaughlin, who used to be a personable and well-liked classical dancer, were supported by the *Herald-American* newspaper, and they attempted to secure a repeal of the city ordinance which permitted the use of vagrant dogs, from the city pound, for medical school purposes.

Through a caretaker who may have simply been a "dupe" for the opposition, pictures of various experiments were made during a six-week tenure, and were captioned in a manner which was intended to mislead and deceive the public. The importance of the situation was sufficient to bring from their daily, busy round, such men as Dr. D. B. Phemister, the Surgeon General of the U.S. Army and Navy, the Director of Public Health and Major General George F. Lull. Fortunately, they had a protagonist in the *Chicago Tribune*, which devoted a great deal of space to printing interviews and editorials, prior to the public hearing.

In 1945, Mrs. Charles M. Petkus, vice-president of the Illinois Citizens Animal Welfare League, spearheaded an attack upon Northwestern University and brought into municipal court, Dr. F. B. Snyder, president of the university, Dr. G. A. Gardner, acting dean of the medical school and Dr. A. C. Ivy of the department of physiology. The grounds for action this time were "unsanitary and filthy conditions" in the animal rooms. The falsity of the charges were established and the case was dismissed, but not without a great deal of effort and loss of time by all of these extremely busy men. The *Herald-American*, adopting the slogan of John Paul Jones, said, "We haven't begun to fight."

Early in 1945, a bill against animal research actually passed the senate of the state of New York. The vote stood thirty-nine in favor of the restricting law, and nine against the law. This was the first time that such a bill had passed one of the legislative bodies in our state, but it was finally shelved in the House Rules Committee, after a bitter contest. However, when the legislature convened in January 1946, one of the first measures to be introduced was the socalled Di Costanzo-Davidson Bill. Mr. Di-Costanzo presented the bill before the senate, and Mr. Davidson was to have done the same before the assembly, but when he became further enlightened as to the aims and purposes, and as to what the bill, if passed, would do to endanger medical progress, he refused to go further with it. However, it was picked up where he had dropped it by a new sponsor, a Mr. Van Duzer. This enterprising gentleman actually presented the bill before the assembly, but after a spirited dispute, the assembly followed the senate in killing both bills on March 14th. This was a narrow escape from the worst kind of "class legislation", the class being soft-headed, faint-hearted and ill-informed sentimentalists, to whom humans are of little importance in the animal world.

In 1945 and 1946, the District of Columbia saw a determined antivivisectionist in the person of Representative Lemke, a republican of South Dakota. He was ably supported by Senator Sanger of North Dakota, who promised him full support, if and when, the bill reached the upper house. Action is still pending, the bill is still alive and will very likely be brought out again during 1947. It calls for a fine

of one hundred dollars to five hundred dollars, and imprisonment of from three to twelve months, or both, for any surgical operation on a dog in the District of Columbia, *for any save curative purposes*. Again, the distinguished professors were called upon to defend the present status. They were Dr. Alfred Blalock of Johns Hopkins, Brigadier General S. Bayne-Jones of the army, Captain Hackenson of the Bethesda Medical Center and Dr. Frederick Brady of the U. S. Public Health Service. They testified as to the value of experimentation in establishing the uses of blood plasma, the technique of blood vessel surgery and data used in the treatment of tropical diseases.

In 1945, the city of Baltimore had a session with those who would prevent by law, the use of live dogs for experimental purposes in that city. Once more, the combined efforts of many prominent physicians and researchers were required to defeat the proposed city ordinance.

Many other American cities, including San Francisco, Cleveland and Boston, have had and are having difficulties defending their scientific workers against malicious attacks. Wisconsin is so troubled, that it has to maintain a permanent lobby (by its medical organizations) to fight such attacks. Therefore, it is unwise to be complacent. The antivivisectionists are a determined group and are operating wherever they can secure a toe hold. Their assertions are based upon: cruelty, moral right, effect on character, no benefit, "man's best friend", and what they regard as the general depravity of any animal researcher.

Our arguments against such regimentation must be based upon the study of function in the lower animals; surgical advancement in nerve, tendon and blood vessel work; transplantation of tissues and organs; the standardization of drugs and the study of new remedies as to potency and effectiveness in bacterial invasions; the standardization of serums, antitoxins and vaccines; the protection of animals themselves against such diseases as rabies, hog cholera and foot and mouth disease; a study of bacterial action, and the means to be taken against it in the living animal. Surgical asepsis and antisepsis were the result of work on animals; vitamins and hormones have been developed by animal studies; in infantile paralysis, the monkey has been of incalculable value in evaluating the cause and effect; cancer research has depended upon mice for much of its results so far established; malaria in all its phases, together with remedies therefore, is best observed in monkeys, dogs, rats and chickens; burns, shock, gas poisoning and other casualties incident to war, have been alleviated through animal experimentation; anesthesia in humans would be unsafe and new agents could not be tried unless animals were available for study; and finally, in World War II, some forty-eight thousand men owe their lives to the discoveries and applications of remedies developed in laboratories since 1920.

To combat the menace, we shall have to use financial measures, educational campaigns, demonstrations and aggressive warfare, "carried to the enemy". Passive resistance is not enough. We must legislate against comprising and defeatist groups who would bind us body and soul against all efforts to obtain medical progress. Moreover, the individual has as his responsibility, at all times and in all places, to make the truth known, and to lay bare the falsehoods and accusations which are now rampant. If we do not do this, we shall be in the position the old anatomists were when they could be burned at the stake, "for desecrating the human body."

Overexertion as an Accident

The main question in a recent action to recover double indemnity benefits provided for in a life insurance policy under New York law, was whether and under what circumstances, overexertion may be determined to be an accident, for the result of which recovery may be had under the double indemnity clause of such a policy. The New York Appellate Courts have not permitted recovery for a loss caused directly and proximately by an act of overexertion "when the act was the natural and customary act of a householder in or about his house, or of a workman within the scope of his duties in his calling." In this case, however, the circumstances were entirely different. The insured, a man of forty-one, apparently in good health, died after slipping and falling against his automobile, while engaged in shoveling snow. He was attempting to extricate the car from a snowbank in which it had become imbedded, as the result of avoidance of a collision with another car on a snowy, windy day. The deceased had been compelled to walk a mile to get the shovel, and was tired and exhausted when he got back. After resting, he began to shovel the snow, which was drifting into the car. While shoveling, he slipped and fell against the shovel or the car. He was helped into the car; in about twenty minutes a passing car undertook to convey him to a hospital, but he died on the way.

The New York Appellate Division affirmed a judgment for the plaintiff. One judge dissented on the ground that the insured's death was claimed to

be the result of overexertion and a fall, and "overexertion is not a cause of death commonly spoken of as included within the meaning of the terms external, violent and accidental means." This judgment has been affirmed by the New York Court of Appeals (Burr vs. Commercial Travelers Mutual Accident Ass'n of America, 295 N.Y. 294, 67 N.E. 2d 248.) The court, in its opinion, treats the problem before it, as being divided into two parts, the primary question here being, whether there was an "accident" within the terms of the policy, and, secondly, whether or not the death was the direct and proximate result of, and caused solely and exclusively by accidental means.

Judge Conway, who delivered the opinion of the court, said: "Legal scholars have spent much effort in attempts to evolve a sound theory of causation and to explain the nature of an 'accident'. Philosophers and lexicographers have attempted definition, with results which have been productive of immediate criticism. No doubt the average man would find himself at a loss if asked to formulate a written definition of the word. Certainly he would say that the term applied only to an unusual and extraordinary happening; that it must be the result of chance; that the cause must be unanticipated, or, if known, the result must be unexpected. We have indicated the 'means' which a jury could have found caused the bodily injuries resulting in the death of the plaintiff's husband, and have pointed out the incidents occurring on that morning which in our opinion would cause the average man to include such means in the term 'accidental' as used in the policy. Here it was not only the result of such incidents which were unexpected, but a jury could find that the catastrophe was brought about by the intervention of unintended and unexpected means, such as the automobile collision, the blizzard and wind storm, a slip or a twist of the body, resulting in a fall and trauma, placing a strain upon the body which the body could not withstand.

"Our guide must be the reasonable expectation and purpose of the ordinary business man when making an insurance contract such as we have here."

"In this state there is no longer any distinction between accidental death and death by accidental means, nor between accidental means and accidental results. A distinction between 'accidental means' and 'accidental results' is certainly not understood by the average man and he is the one for whom the policy is written."

On the second point, the Court of Appeals said: "It was made clear to the jury (in the trial court's charge) that if the death was the result of a preexisting disease, even though that may have been aggravated by the accident, there could be no recovery, because then the accident could not be considered as the sole and exclusive cause of death." By their verdict in favor of the plaintiff, the court said, "the jury must have found that there was no preexisting disease and that the deceased died 'from overexposure or overexertion, or by slipping or falling against the car or by a combination of all three' without the existence of any preexisting disease".

Commenting upon the use of the word "overexertion", by the trial court in its charge, the Court of Appeals said: "In this state we have not permitted recovery under a policy insuring against a loss 'which is the direct and proximate result of and which is caused solely and exclusively by external, violent and accidental means' when the act was the natural and customary act of a householder in or about his house, or of a workman within the scope of his duties in his calling. (citations omitted).

"It seems quite clear here, however, that on the facts presented, a chain of causation was set in motion beginning with the automobile accident in the course of and brought about by travel in a very heavy snow and wind storm, followed in turn by what may be termed an emergency, resulting from the fact that the deceased had his wife and thirteen year old son with him, at a time when the cold was bitter and the automobile was being filled with sifting snow, and it was necessary for the deceased to act to protect his family. This case is no more comparable to the conventional overexertion case than if the deceased had, by an accident, been thrown into a pit and in endeavoring to clamber out in order to save his life, had died by reason of overexertion in climbing, or had been thrown by an accident into the water and had died from overexertion in attempting to swim ashore".

Chilblains

Chilblains are common. They are not dangerous but troublesome and sometimes invaliding, and they cause a loss of efficiency as can well be imagined. During the war, they were responsible for a serious loss of efficiency among members of the British Auxiliary Territorial Service. They are, or at any rate supposed to be, more frequent among women than among men. An article in the *Lancet,* November 9, 1946, on "Chilblains in Servicewomen" by Dr. Albertine L. Winner, M.R.C.P., late lieutenant colonel, and E. S. Cooper White, M.A., late captain, Army General List, deals with the subject exhaus-

tively, in regard to women under forty, but not in respect to men. The literature of chilblains is enormous but not satisfactory, although it is generally agreed that the main etiological factor is cold. Some persons are more susceptible to this complaint than others, but this is true with many diseases and affections. The summary of the article is as follows: An analysis was carried out on the answers to 13,003 questionnaires filled in by A.T.S. officers and auxiliaries, concerning the incidence and natural history of chilblains. When the incidence at different ages was calculated, it was found that at least half the women would have chilblains by the time they were forty years old, but the incidence rises steadily up to the age of forty. The most likely age for the beginning of chilblains was fifteen to seventeen and its disappearance occurred at twenty to twenty-two years. There was also a tendency to have a clear interval between the ages of twenty-five and thirty. There is some evidence that in this group at least, chilblains were more prevalent during the war years, though not during war service. Office workers have a higher incidence than those in an active occupation, but outdoor exposure does not seem to have any effect. Office workers tend to get chilblains on their hands, whereas those whose work involves much standing, get them on their feet. There is some indication of familial influence on chilblains. Many remedies are reported as being beneficial, but it is concluded that none are specific. After all has been said that can be said of this affection, is it not mainly due to sluggish peripheral circulation? They appear most often after exposure to cold and in elderly persons, and children in particular, whose circulation is naturally slow. The lesions are salmon pink on the fingers, toes, lower parts of the legs and the ears. When the hélices of the ears are attacked as they are attacked sometimes in old people mainly, considerable loss of tissue may result. As said before, there is no specific treatment and perhaps some of the ancient folk lore remedies are as effective as any. Some cases improve by the internal administration of calcium salts and/or cod liver oil.

Dicumarol

An educational exhibit on dicumarol will be displayed by Schieffelin & Co., New York, N. Y., at the third annual exhibit of the New York Academy of Medicine. As an aid to physicians, this exhibit will list the indications and fields of use, contraindications and a chart illustrating the method and control of dicumarol therapy. A detailed brochure on dicumarol will be available to the visiting physician.

First Commercial Sale of Rare Carbon Isotope

The Eastman Kodak Company has announced that the first shipment of Carbon 13, the rare new isotope used by medical science to probe secrets of the life processes, was recently sent from the Kodak Research Laboratories to New York's Memorial Hospital. Company officials said that they believed the shipment marked the first sale of the isotope produced on a commercial basis.

Valued at about two hundred dollars, the shipment consisted of one-half gram of Carbon 13 in the form of twelve grams of potassium cyanide containing the carbon isotope in a concentration above twenty percent. Dr. C. E. K. Mees, director of Eastman Kodak research, said that Dr. C. P. Rhoades, chairman of the National Research Council's committee on growth, would receive the shipment in New York. Dr. William O. Kenyon, head of the Rochester laboratory's organic chemical department, explained that high concentrations of the valuable isotope will be sold exclusively to organizations cleared by the Research Council for study of cancer and metabolic diseases. He said that more general distribution of intermediate concentrations will be made to other research units.

Dr. Mees said that before long, the company will further facilitate the application of isotopes to research work, by providing a variety of compounds with isotopes already inserted. "While at present we are producing Carbon 13 in the form of potassium cyanide, before long we will make considerable amounts of synthetic organic compounds containing the carbon isotope. It is expected that methanol will be one of the first of these compounds," Dr. Mees said.

Carbon 13, obtained by separating the one-in-a-hundred heavy carbon atoms from ordinary carbon, is expected to prove of greatest value as a "tracer" in biological research. When fed in compounds to animals and absorbed by living tissues, the heavy carbon becomes involved in the life processes in the same way as ordinary carbon.

Ordinary carbon, however, cannot be followed in the chemical changes of life, whereas Carbon 13 can easily be traced by means of an electrical instrument called the mass-spectrometer, which measures differences in masses of individual atoms. Used as a "tracer," the carbon isotope is especially important in studies of growth and metabolism of cells, including the abnormal cell growth in cancer.

News Items

American Cancer Society.—Dr. Fred Karush, Elmhurst, N.Y., has been awarded a three year senior fellowship by the American Cancer Society, for cancer research at the New York University College of Medicine. Dr. Karush began his work on January 1, 1947, under the direction of Dr. R. Keith Cannan, department of chemistry, the College of Medicine.

Dr. Karush, for the last five years a researchist with the Du Pont Chemical Company studying the physical techniques of color pigments, will be associated with the New York University for the first time. The stipend granted by the cancer society for the first year is $5000. An additional $1000 a year will be awarded to defray laboratory expenses.

Pharmacology Grant.—The First Texas Chemical Manufacturing Company, Dallas, Texas, has awarded a grant of $5,000.00 to the Southwestern Medical Foundation for carrying on research work in the department of pharmacology.

The foundation has been the recipient of many grants from pharmaceutical houses with their headquarters in other parts of the country, but this is the first received from a pharmaceutical company with national headquarters in the Southwest.

In presenting the grant, V. M. Payne, president and general manager of the company, said that his organization, which deals largely with the medical profession of the Southwest, is greatly interested in cooperation with the Southwestern Medical Foundation and College, in behalf of medical research in, and for this area.

Rosenstock Memorial Foundation.—The Rosenstock Memorial Foundation, Inc. is offering three fellowships of $2,000 per annum, renewable upon reapplication and favorable reconsideration for an additional year. The grants are limited to the support of individual medical research, to be conducted in hospitals with medical school affiliations in any of the five boroughs of New York City. Fellowships may be granted for either fulltime or part time medical research.

Fellowships will be limited to those who apply within three years of the completion of their internship or residency (excluding the time spent in military service), except that a recipient of the fellowship may reapply for one renewal of the grant. Applications must be endorsed by the director of the hospital where it is proposed that the research shall be conducted, and then forwarded by the endorser to the foundation at 42-16 West Street, Long Island City 1, N.Y., by October 1, 1947. The announcement of grants will be made in December, 1947, and the funds will then be turned over to the hospitals involved.

New Technique for Fractures.—According to an announcement made by the Philips Laboratories, Inc., New York, N.Y., an article which outlines a new operative method, wherein the parts of the broken bone are joined together by the hammering of a hollow steel pin, after the previous drilling-in of a guiding needle, appears in issue No. 8 of *The Philips Technical Review*, recently received from overseas.

This procedure makes sure that the pin will lie in the right position, which will have been previously determined by means of x ray photographs. Compared with other devices, the new directing instrument has the advantage that all necessary adjustments (as predetermined from x ray photos) can be made before the actual operation is begun. This considerably shortens the time needed for the operation; moreover, except for the conductor of the guiding needle, the instrument does not need to be sterilized.

Series of Penicillin Booklets.—The first in a series of concise, ready-reference booklets entitled *Penicillin Paragraphs*, has been mailed to all active physicians in the United States by Schenley Laboratories, Inc., to help disseminate the significant, clinical experience in the use of this wartime-developed medicine.

A new edition will be issued each month, with each booklet devoted to clinical material bearing on the treatment of a specific disease. The initial issue of *Penicillin Paragraphs* deals with the use of penicillin in pneumonia. By filing each issue, physicians can build an indexed file of compact, authoritative reports on a wide list of diseases amenable to penicillin therapy.

A further informational service offered by the company is a comprehensive penicillin dosage chart, available to all physicians who request it.

National Mental Health Foundation.—The National Mental Health Foundation has recently announced that it has completed the production of its electrically-transcribed series of radio programs, entitled, "For These We Speak". These eight plays, dealing with various aspects of mental illness, are now available for sponsorship over local radio outlets by mental hygiene societies and similarly concerned organizations.

The general aim of the series is the education of the American public to a sympathetic understanding of the mentally ill. Specifically, each program is a dramatic treatment of one particular problem in this field. Each play is approximately thirteen and-a-half minutes in length, allowing the local sponsoring organization sixty seconds for a message of local interest. Mental hygiene societies, public health agencies and the civic organizations desiring to assist in the sponsorship of this series over radio stations in their communities, are invited to address their inquiries to the radio section of the National Mental Health Foundation, Box 7574, Philadelphia 1, Pa.

New Hearing Aid.—A new discovery, which will revolutionize the hearing aid industry and which consists of the tiniest instrument yet developed, was revealed by Stanley Osserman, chairman of the Board of Acousticon International. This scientific development is the result of a battery used in proximity fuses and finger nail sized electronic tubes which were created as a result of war experiences. The world's tiniest hearing aid weighs only five and one-half ounces, as compared with the first hearing instrument which weighed four pounds. The new instrument is half the length of a modern fountain pen and almost as thin.

Robert Trubek Fellowship.—Dr. Currier McEwen, dean of the New York University College of Medicine, recently announced that Dr. Norman Spitzer, Yonkers, N.Y., has been appointed the Robert Trubek fellow in rheumatic disorders for 1946-47.

The fellowship, which carries a stipend of $2,500, provides a year of supervised research and special clinical training in rheumatic disorders at the New York University College of Medicine and the society of the fourth division, Inc., of Bellevue Hospital.

Established last spring by Robert Trubek, East Rutherford, N.J., the fellowship in rheumatic disorders is open to physicians with at least two years of previous training in internal medicine, or its equivalent.

Tumor Clinic in Utica.—According to *Health News*, December 9, 1946, the opening of a new tumor clinic in St. Elizabeth Hospital, Utica, N. Y., under the auspices of the American Cancer Society, was recently announced. The clinic is for the diagnosis and treatment of cancer and allied diseases. The medical staff is composed of members of the medical society who have volunteered their services and have been selected for three-month periods. The Women's Auxiliary of the medical society has volunteered its services for nursing and clerical aid.

Patients will be examined and treated upon reference, in writing, by the family physician or another competent agency. If examination, only, is requested, the case will be sent back to the referring authority with recommendations for disposition; otherwise, examination and treatment will be given.

The fee for a clinic visit will be one dollar. This charge may be waived at any time at the discretion of the clinic director. Additional charges will be made for x ray and laboratory studies, or x ray treatments by the hospital. Arrangements for the payment of such expenses for those unable to do so themselves are being made.

The establishment of the Utica tumor clinic raises the total number of such clinics in upstate New York to forty.

Friday Afternoon Lectures.—Beginning with February 28th through March 14, 1947, the following lectures in the twenty-first series of Friday Afternoon Lectures will be given at the New York Academy of Medicine:

February 28: Use of male sex hormones in clinical medicine, by Sidney C. Werner, associate in medicine, College of Physicians and Surgeons, Columbia University;

March 7: Psychosomatic medicine, by George E. Daniels, clinical professor of psychiatry, College of Physicians and Surgeons, Columbia University and

March 14: Anemias with especial reference to treatment, by Nathan Rosenthal, hematologist and associate in medicine, The Mount Sinai Hospital; assistant clinical professor of medicine, College of Physicians and Surgeons, Columbia University.

Lederle Laboratories Height Chart.—An aid to the physician with a large pediatric practice, is the cerevim giraffe, an unusual height chart now being offered to the medical profession by Lederle Laboratories, New York, N.Y., in connection with their precooked cereal, cerevim. Designed to enlist the cooperation of mothers and their children in keeping the valuable records of progressive development, the chart is an amusing giraffe, forty-two inches high, whose elongated neck is marked off in inches and has enough space for correlating the age and weight with the height.

Cerevim giraffes can be obtained in quantities by physicians, for distribution to private patients, and also for groups such as nursery schools and children's homes. Charts, and also samples of cerevim, are obtainable by writing to Lederle Laboratories Division, New York 20, N.Y.

First Inter-American Congress on Brucellosis.—According to *Health News*, December 9, 1946, the fifth congress for the study of brucellosis was recently held in Mexico City under the auspices of the Mexican National Brucellosis Commission, the Mexican Society of Tropical Medicine and the Organization Committee of the Congress. This meeting became known as the First Inter-American Congress on Brucellosis.

Organization of the Inter-American Congress on Brucellosis was completed under the presidency of Dr. Evans. Other members of the organization committee were Dr. M. Ruiz Castaneda, Mexico; the late Dr. Salvador Mazza, Argentina, and Dr. Huddleson. The committee, serving with the president, is empowered to bring to the attention of the proper division of the United Nations the importance of forming a world organization to deal with the brucella infection in animals and man.

The second Inter-American Congress on Brucellosis will be held in Argentina in 1948, probably in April.

Osteopathy. — The Veterans Administration has recently announced that arrangements have been completed for the appointment of doctors of osteopathy to serve in the Veterans Administration's department of medicine and surgery.

The appointments will be made in compliance with Public Law 293, Seventy-ninth Congress, which authorizes the Veterans Administration to hire doctors of osteopathy to work with the veterans.

A doctor of osteopathy, to be eligible for appointment, must: 1. be a citizen of the United States; 2. hold a degree of doctor of osteopathy from a college or university recognized by the Veterans Administration; 3. have completed an internship satisfactory to the Veterans Administration; 4. hold a license to practice osteopathy in one of the states, territories or the District of Columbia; 5. meet with the Veterans Administration's prescribed physical standards.

Doctors of osteopathy interested in securing positions with the Veterans Administration should forward their applications to the deputy administrator of the Veterans Administration branch office having jurisdiction over the area in which the applicants desire to work.

Schering Award for 1946.—The Schering Corporation, Bloomfield and Union, N.J., has recently announced the winners of the 1946 Schering award for the best essays on the subject of "The rôle of hormones in sterility". In the selection, Dr. I. C. Rubin, clinical professor of gynecology, Columbia University College of Physicians and Surgeons, New York, N.Y., served as one of the judges; together with Dr. Ephriam Shorr, associate professor of medicine, Cornell University Medical College, and Dr. Sidney C. Werner, associate in clinical medicine, the College of Physicians and Surgeons.

Mr. Bent G. Boving, Lansdowne, Pa., a student at Jefferson Medical College of Philadelphia, was selected as the winner of the $500.00 first prize. The second prize of $300.00 was awarded to Mr. William O. Maddock, Portland, Ore. Mr. Maddock is a student at the University of Oregon Medical School.

Two papers were adjudged by the judges as equal in merit and deserving of the third prize. As a consequence, two identical third prizes of $200.00 each, have been awarded to the following contestants: Mr. Lionel M. Mapp, McGill University Faculty of Medicine, and a resident of Montreal, Quebec, Canada, and Mr. Stonewell B. Stickney, Mobile, Ala. Mr. Stickney is a student at Tulane University of the Louisiana School of Medicine. Forty-four of the entrants were designated an honorable mention. Although it was not previously announced, each of these contestants will receive as a special award, a stethescope in a leather case.

Announcement will be made in the near future of the subject for the Schering award for 1947.

Personal.—Dr. Paul Budd Magnuson, professor of surgery and chairman of the department of bone and joint surgery, Northwestern University Medical School, Chicago, Ill., has been appointed as acting assistant medical director for research and education of the Veterans Administration.

Dr. Adolph G. Kammer has been appointed to the newly-created post of director of medical services of Schenley Distillers Corporation, according to a recent announcement.

Miss Mary P. Connolly, director of health education, school of public health, University of Michigan, was the recipient of the Elizabeth Severance Prentiss National Award in health education, presented by the Cleveland Health Museum. Miss Connolly was selected for her pioneer work in the field for which the award was made.

Dr. Karl F. Meyer, director of The Hooper Foundation and professor of bacteriology, University of California, received the Sedgwick Memorial Medal for 1946 for his work in "revealing the secrets of diseases transmitted by animals to man and his vigorous and enlightened service in building up the public health program of the nation."

Francis R. St. John, formerly chief of the circulation department of the New York City Public Library, has been appointed director of the newly organized Veterans Administration library service. He assumed his new duties on January 1, 1947, succeeding Miss Elizabeth Pomeroy, acting director of the library service, who retired in December.

Dr. John K. Miller has been appointed associate director of the Division of Laboratories and Research to succeed Dr. Mary B. Kirkbride who retired July 1st.

Dr. Robert E. Plunkett, head of tuberculosis control, New York State Department of Health, has been appointed as a member of the committee on tuberculosis of the division of medical sciences of the National Research Council. Other organizations of national scope to which Dr. Plunkett has been appointed recently, include the sanatorium planning and the budget and program committees of the National Tuberculosis Association, the committee on tuberculosis in custodial and penal institutions of the American Trudeau Society, of which he is chairman, and the medical advisory board of that society. Dr. Plunkett is in charge of the expanded program for the eradication of tuberculosis in New York State by 1965.

Dr. Kenneth Wade Thompson, formerly managing editor of the *Journal of Clinical Endocrinology* and clinical professor of surgery at Tufts College Medical School, has joined Roche-Organon, Inc.

Dr. I. Newton Kugelmass has recently been appointed as consultant nutritionist to the New York departments of health and hospitals.

Three Bicentennial Anniversaries—Pinel, Frank, Cruikshank

HYMAN I. GOLDSTEIN, M.D.,
Camden, N.J.

Phillipe Pinel (1745-1826) was born into poverty in 1745. He was a pupil of Barthez (1734-1806) of Montpellier, who followed Bordeu (1722-1776) in his views on *"vitalism"*. Pinel studied the workings of the brain and observed that in certain conditions of mania or partial insanity, memory, judgement, will or imagination were abolished or suspended, and other mental faculties were preserved. Earlier, Thomas Willis (1621-1675) considered special functions of certain parts of the brain and was a pioneer in cerebral localization, although it was Pinel, at the risk of his life, who first "struck off the chains" from forty-nine insane patients at Becêtre in Paris (1793, 1798). Esquirol (1772-1840), at the Salpêtriére, continued Pinel's ideas and reforms for the humane care of the insane. Pinel published his *"Traite Medico-philosophique sur l'alienation mentale"* in 1801, and he was among the first in France to promote Jennerian vaccination (1798). Sauvages (1706-1767), a forerunner of Pinel who followed Stahl's *"Animism"* and *"Soul"*, did not influence Pinel in originating his *"Realism."* Pinel was somewhat of a Barthez vitalist, and a follower of the great French philosopher Condillac (1715-1780). He preferred the analytical method in medicine, and believed in analyzing the various phenomena and symptoms.

Johann Peter Frank (1745-1821) was born into poverty and at an early age was abandoned by his father. He was a professor at Pavia, Göttingen and Vienna. He was also the author of a *"System einer vollstandigen medizinischen Polizey"* (1777-1788), which contained important principles of state hygiene. He believed that the health of the public was the responsibility of the state, and he was interested in the education of children and in school-hygiene. He encouraged the idea that the government was at all times responsible for the public health, and therefore, was one of the early supporters and promoters of preventive medicine. He was one of the first physicians to emphasize the importance of diseases of the spinal cord (1792), He observed and defined diabetes insipidus (1794) and wrote on the subject of therapeutics, *"De curandis hominum morbis epitome"* (Vienna, 1792-1821). Frank was the pioneer, 'modern' hygienist and public health authority. He was one of the greatest practitioners and teachers of his time, truly a self-made man!

William C. Cruikshank (1745-1800) of Edinburgh, succeeded William Hewson (1739-1774) as William Hunter's (1718-1783) assistant, and continued Hunter's investigations of the lymphatic system. Cruikshank studied the physiology of absorption (1778-1786), and published his "Anatomy of the absorbing vessels of the human body" in 1786. He studied the regeneration of divided nerves (1776), and discovered that severed nerves will grow together. He studied the passage of the impregnated ovum through the Fallopian tube (1778), and wrote *Experiments upon the insensible perspiration of the human body* (1778), demonstrating that the skin (like the lungs) gives off carbon dioxide. It was later demonstrated by Gustav Magnus that all tissues assimilate oxygen and give off carbon dioxide. He demonstrated albuminuria (1797) in dropsical fevers.

1425 Broadway.

Television in Tuberculosis Campaign

According to *Health News,* December 23, 1946, television was enlisted in the campaign against tuberculosis, when the story of what a community could do in the prevention and control of the disease was presented over a local station in Schenectady, N. Y.

Entitled "The lamplighter" and narrated by a live figure dressed like the lamplighter of this year's Christmas Seals, the presentation was highlighted by the appearance of Dr. Edward S. Godfrey, Jr., commissioner, New York State Department of Health, who outlined the department's tuberculosis eradication program. View by the general public was made possible by arrangements with department and music stores. Using live action and movie film, the television presentation dramatized the dangers of tuberculosis, how the disease may best be treated in a modern sanatorium, and how it can be discovered by mass radiography.

The need for the establishment of administrative machinery to assure adequate treatment, follow-up and the rehabilitation of tubercular patients was emphasized by Dr. Godfrey. He pointed out that one of the most important aspects of the new state tuberculosis control program is the complete elimination of the means test; after January 1, 1947, any patient with tuberculosis who needs hospital care, may obtain that care without cost. The state is providing financial aid to municipalities throughout the state, including New York City for the hospital care of patients with tuberculosis, as well as conducting its own four tuberculosis hospitals in upstate New York, to supply those areas which do not have local tuberculosis hospitals.

Making chest x rays available to everyone in the state, is another important objective of the new tuberculosis control program, Dr. Godfrey continued. He stressed, however, that finding a case is only the beginning and added, "Adequate care of the individual found to have tuberculosis, must be provided so as to give that individual the best possible chance for rapid recovery and to keep others from catching the disease from him. This involves the proper follow-up of individuals found to have tuberculosis.

"Thus, another important aspect of the expanded public health program in New York State is to facilitate the development of adequate, local health departments by establishing and helping to improve fulltime county health departments and the services of city health departments."

Letter From Britain

(From Our Own Correspondent)

At the time of writing, the situation here in Britain in regard to the medical profession is as it was. That some radical but not revolutionary changes will come, seems probable; however, it appears evident that there will be no great upheaval. In the meantime, students of medicine at the universities and medical schools are enrolling in large numbers. Some who were studying medicine when the war came, enlisted in the armed forces; those who emerged from the war sound, or partly so, in body and mind will now finish their course; many others who fought have chosen medicine as their profession and the entries into medical schools on the part of such men have been large.

Chair of Human Nutrition, London School of Tropical Medicine

Dr. B. S. Platt, director of the human nutrition research unit of the British Medical Research Council, has been appointed to the Chair of Human Nutrition, tenable at the London School of Hygiene and Tropical Medicine.

Dangers of Raw Meat

The British Ministries of Food and Health have sent out warnings against eating pork, pork sausage, ham or any other pork product, unless it has been thoroughly cooked. Attention is also called to the dangerous practice of spreading raw sausage meat on bread and recalls that this habit has been a potent cause of trichinosis.

Recent Appointments to the University of Leeds

Recent appointments to the University of Leeds include the following people: Dr. H. T. Rogers to be the Nuffield Research Fellow in oral biology; Dr. A. B. Moggy to be the Brotherton Research Lecturer in physical chemistry in the department of textile industries, and Dr. H. M. Tattersall to be the fulltime lecturer in medicine.

Chair of Medicine, British Postgraduate Medical School

Dr. John McMichael, formerly a lecturer in human physiology at Edinburgh University, and since 1936, Johnstone and Lawrence Research Fellow of the Royal Society, and honorary assistant in the Royal Infirmary, Edinburgh, has been appointed to the University Chair of Medicine, tenable at the British Postgraduate Medical School.

Dr. C. T. Mackenzie Elected a Fellow of the Royal Society

Dr. C. T. Mackenzie, president of the National Research Council of Canada, has been elected a Fellow of the Royal Society of London. He was elected under a statute of the Royal Society which provides for the election of persons, who have either rendered conspicuous service to the cause of science, or whose election would be of signal benefit to the society.

Atomic Energy Act

An Atomic Energy Act has become law in Britain, and some of its provisions may affect the work of scientific men and of medical scientists. Most of its clauses will have no immediate effect, and until the act has been made more clear, it is useless to discuss any of its provisions. However, the British Atomic Energy Act is being criticized for its negative aspect and, it is said that from this point of view, it differs from the American Atomic Energy Bill.

Anniversary Meeting of the Royal Society of London

The anniversary meeting of the Royal Society was held in London on November 30, 1946, where the president, Sir Robert Robinson, gave his presidential address. Referring to the danger to scientific ideals and integrity in the conceptions of total war, he pointed out that scientists are confronted with a dilemma; a conflict between their ideals of service to humanity and their duty as citizens of a democratic community, which can only be resolved by the establishment of real friendship and accord among nations. Speaking for himself, he said that all men of science should strive to promote international peace and to outlaw all methods of warfare, which by their nature, involve "total war".

Faraday Lecture of the Chemical Society

Sir Robert Robinson, president of the Royal Society of London, will deliver the Faraday Lecture of the Chemical Society on July 16, 1947, during the society's centenary celebrations. The Faraday Lectureship was founded in 1867, in memory and honor of Michael Faraday. It is the highest honor the Chemical Society has to give, and Sir Robinson will follow many great men. The list of names of previous lecturers, include Duman, Cannizzano, von Hoffman, Wurtz, Helmholtz, Mendeleff, Lord Rayleigh, Ostwald, Fischer, Richards, Arrhenius, Millikan, Willstätter, Bohr, Debys and Rutherford. The lecture will form the chief event of the Chemical Society's celebrations.

Goethe's Essay on Metamorphosis of Plants

Goethe's *Essay on the Metamorphosis of Plants* (1790) has been critically translated by Dr. Agnes Arber. Goethe's essay has been translated several times, never better than by Dr. Arber. It may be stated that Goethe in this essay concluded that all parts of the plant except the stem are modified leaves. In his essay, he argued deductively as to the fundamental unity of leaf, flower and fruit and that all plants are descended from an archetypal form. Goethe was one of the pioneers of evolution, the first to use the term "morphology" and the discoverer in 1786 of the intermaxillary bone. Independent of Oken, Goethe put forth the theory that the skull was made up of modified vertebrae, and before Savigny, he observed that the jaws of insects were modified limbs. Goethe was a genius and a very great poet; also his views on botany were highly suggestive if not always absolutely sound. Dr. Agnes Arber's translation and criticisms of Goethe's essay are most illuminating.

Book Reviews

Gynecology

A Textbook of Gynecology. By ARTHUR HALE CURTIS, M.D., professor and chairman of the department of obstetrics and gynecology, Northwestern University Medical School; chief of gynecological service, Passavant Memorial Hospital, Chicago, Ill. Fifth edition. With 455 illustrations including 36 in color. Philadelphia and London: W. B. Saunders Co., 1946. Pp. xiv + 755. Price $8.00.

The first edition of this book was published in 1940. Since then, other editions have been brought out consistently every four years. In this printing, all chapters save a few have been extensively revised. The author particularly stresses the section on ovarian tumors and devotes some seventy-five pages to a complete discussion of them. Their complexity has led to the conclusion that they cannot be classified pathologically. This makes little difference, since mere enumeration of the recognized clinical varieties suffices for practical purposes. However, it is now well recognized how extremely important the condition of the ovaries is to a woman's general health, since these are subject to even greater deviations from normal than the uterus itself.

Gonorrhea in the female, it is pleasant to note, "has become relatively infrequent in gynecological practice" (p. 151). This, the author thinks, is due to "broader education in sex problems and awakened realization to the seriousness of the disease." It is implied that infected persons are now exercising care not to pass the disease on to others. This is, indeed, a highly desirable awakening of conscience which has not previously been notable; however, gonorrhea still remains the most common cause of sterility. Concerning the use of penicillin, Dr. Curtis recommends a much larger dosage in gonorrhea than has been the rule hitherto. He administers 25,000 Oxford units gluteally, every three hours, and says that 300,000 units may be necessary to effect a cure. Much is to be hoped for through oral administration, but this is still in an experimental stage as to its ultimate value. Calcium carbonate is used to buffer the gastric juice, but the mould is still susceptible to destruction even when used in dosages of 100,000 to 200,000 units daily.

Dr. Curtis' latest revision still maintains its high level of excellence.

Obstetrics and Gynecology

Synopsis of Obstetrics and Gynecology. By ALECK W. BOURNE, M.A., M.B., consulting obstetrical surgeon, Queen Charlotte's Hospital, London; obstetrical surgeon, St. Mary's Hospital, London. Ninth edition, fully revised with numerous diagrams. Baltimore: The Williams & Wilkins Co., 1945. Pp. vii + 500. Price $5.00.

The ninth edition of this extremely useful handbook, states in a simple and concise manner, the principal points of obstetrics and gynecology for students preparing for examinations. It is intended that the book should serve as a useful supplement to, and not as a substitute for, the ordinary textbooks; in order that the subject may be quickly revised. Important points for examination purposes have been emphasized, and literary expression has been sacrificed for the sake of brevity and conciseness. The sections on treatment have been given in more detail and rendered as practical as possible, in the hope that the work may also prove of use to the general practitioner.

In all controversial matters, extreme views have been avoided, and the text follows the usually accepted opinion as set forth by Eden, Galabin and Blacker, Herman, Munro Kerr and Whitridge Williams.

As in previous editions, there have been many alterations, both by addition and suppression. On this occasion, revision has been even more thorough. For the purpose intended, the book is excellent.

Penicillin

Penicillin. Its Practical Application. Under the general editorship of SIR ALEXANDER FLEMING, M.B., B.S., professor of bacteriology, The University of London, St. Mary's Hospital, London. Illustrated. Philadelphia: The Blakiston Co., 1946. Pp. x + 380. Price $7.00.

Sir Alexander Fleming was quite recently in this country and received honorary degrees from Princeton and Columbia Universities. In his preface, he modestly states that when asked to write a book on penicillin he refused; first, because he is a laboratory man and not a clinician with experience in the use of his discovery, and secondly, because he had "too many commitments to do justice to such a book." However, when he was told that he might supervise the essays of co-contributors, he assented, and so we have the composite study of some thirty experts who write concerning the chemistry, pharmacology, manufacture, bacteriological control, methods of administration, prophylactic use, and use of penicillin in the presence of infections.

Dr. Fleming says that, because of its scarcity, penicillin may not have been used adequately during the war, and so the results were uneven and uncertain. It may be wasteful to give more than is required for therapeutic effect, but one cannot prescribe too much, with respect to toxicity, since its toxicity is about *nil*. Ordinarily, one may give 15,000 units every three hours, intramuscularly, day and night, until improvement is noted; then reduce the frequency as common sense dictates, but twice as much may be administered with safety. The general rules are quite simple, but one should bear in mind that there is quite a list of conditions wherein no good result can be hoped for. This is the "Insensitive List" and includes most of the viruses, yeast, monilia and moulds. It is useless in typhoid, cholera, tuberculosis, Friedländer's pneumonia, brucellosis and in the presence of Bacillus pestis. There are, doubtless, other conditions in which penicillin will not prove satisfactory; the only point is, that we must not place a dependence upon it, where it should not be employed.

This book is a useful guide in administering an amazingly useful drug.

Physical Medicine

The 1945 *Year Book of Physical Medicine.* Edited by RICHARD KOVACS, M.D., professor of physical medicine, New York Polyclinic Medical School and Hospital. Illustrated. Chicago: The Year Book Publishers, 1946. Pp. 400. Price $3.00.

This year book presents the new methods of physical rehabilitation applied to war casualties and civilians. The scope of the text ranges between physical therapeutic methods and applied physical therapy. In the former, there is a review of the literature on thermotherapy, electrotherapy, hydrotherapy and mechanical therapy; while the latter part of the book is devoted to the application of newer methods of specific disease entities.

Blood

Disorders of the Blood. Diagnosis, Pathology, Treatment and Technique. By SIR LIONEL E. H. WHITBY, M.D., Regius Professor of physics, University of Cambridge; and C. J. C. BRITTON, M.D., assistant pathologist, The Bland-Sutton Institute of Pathology, The Middlesex Hospital. Fifth edition. Illustrated. Philadelphia: The Blakiston Co., 1946. Pp. xii + 665. Price $10.00.

This new edition presents the quick changing views on the Rheusus Factor, hematological terminology and the origin and development of blood cells. Advances in the mechanism and management of hemolytic anemia and the anemias of infancy and childhood have been included, and the newer procedures in hemagglutination, blood transfusions and marrow punctures have been simplified. The book thus becomes a comprehensive manual of blood disorders devoid of controversial matter. Emphasis is placed on the rarity of primary diseases of the hemopoietic system, and the predominence of systemic disorders reflecting changes in the peripheral blood. Summaries have been added after each chapter to crystallize the subject matter.

Diabetes

Diabetes. A Concise Presentation. By HENRY J. JOHN, M.A., M.D., Lieut. Col., Medical Corps. Illustrated. St. Louis: The C. V. Mosby Co., 1946. Pp. 300. Price $3.25.

This is a commonsense, practical book based on some twenty-five years of "specializing" in diabetes, especially in children, which in any case always affords a good background for a knowledge of disease in adults. Dr. John has for years maintained a diabetic clinic for children near Cleveland, and has planned their lives so that they can take part in all the normal activities at school and at play without becoming obsessed with the idea that they are "not normal".

Obesity, the author says, is a very likely indication of diabetes, present or to come. There is no excuse for overeating and getting into diabetic form, even though good luck may see one through many years of indulgence. He might also have added that if such "too fat" conditions continue long enough, the overburdened heart or kidneys may go on strike. The fat which one sees on the body is not nearly so important as the fat one does not see in and around the vital organs. The observation is made that the University of Liege recorded some facts in reference to overnutrition and diabetes. In the early period of German occupation (1940-1942) there was a sharp decline in diabetes incidence, but with the coming of the black market this incidence was greatly increased. (This fact is noted in the preface by Dr. William C. Middleton, professor in the medical school, University of Wisconsin.)

Dr. John defines diabetes as "a disturbance of carbohydrate metabolism . . . inability of the body to fully metabolize carbohydrates . . ." If the carbohydrates cannot be fully utilized or burned up, glucose accumulates in the blood and other tissues, with resultant hyperglycemia and glycosuria.

The chapter on "Prevention" is important and instructive, bearing in mind that "babies may be born with diabetes". Heredity then plays a part under the Mendelian recessive law, and the alert pediatrician who has a small child under his care for an acute infection, for example, will do well to think of the parents and grandparents as providing a weak susceptibility to disorders of metabolism.

Embryology

Human Embryology. By BRADLEY M. PATTEN, professor of anatomy, the University of Michigan Medical School. With 1366 drawings and photographs, including 53 in color. Philadelphia and Toronto: The Blakiston Co., 1946. Pp. xv + 776. Price $7.00.

For years, medical students have looked upon anatomy as a "dry" subject, especially socalled descriptive anatomy as opposed to work in the dissecting room. Embryology as a specialized form of anatomy in its very beginning, does not make easy reading; therefore, since most of us learn chiefly through visualization, Dr. Patten has given a great deal of thought to figures, drawings and plates, in order to illustrate his subject. He assumes that in his premedical course, the student has been taught at least the rudiments of embryology and histology; therefore stress has been placed upon the practical side of this science in its relation to other related courses in medicine. Anomalies seen in gross anatomy began with some deviation from the embryological pattern, and so a thorough knowledge of the cells, tissues and organs helps the physician to understand what is met with in general practice. The functional correlations have been especially emphasized in dealing with the nervous and circulatory systems. These two, one as coordinator and the other as purveyor, are so intimately inter related, that their structural plan, (must be), interpreted from the functional standpoint.

This is not a laboratory guide. The bookshelves are replete with such manuals, but chapters on "Early differentiation of the body and establishing of organ systems" have been written with a view to the correlation of the text and laboratory study.

The establishing of organ systems on the part of nature and their mutual interdependence, supplies the reason for a book of this kind, based as it is upon original study and research during many years of devoted service.

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FEBRUARY 1947

Medicolegal Notes

Damages

An eleven thousand dollar award to a forty year old switch foreman on a railway, was given for injuries which included the fracture of the left heel bone and compression fractures of the first and fourth lumbar vertebrae. It was held, although apparently large, not excessive in the light of the evidence, in an action under the Federal Employers' Liability Act and the Safety Appliance Acts, Clarke vs. Chicago & N. W. R. Co., Federal District Court for Minnesota, 63 F. Supp. 579.

Practicing Without a License

The Illinois Appellate Court, People vs. Rongetti, 328 Ill. App. 124, 67 N. E. 2d 218, held that any information alleging that the defendant diagnosed or attempted to diagnose an ailment as kidney trouble, and prescribed distilled water therefore; and that the defendant maintained an office equipped with a stethoscope, blood pressure apparatus, a physicians' examining table, sterilizing cabinets and bottles containing unknown ingredients, was sufficient in a prosecution for practicing without a license.

Hospital's Liability for Substitute Intern

A patient in the dental clinic of a hospital society in Connecticut had a tooth extracted by a substitute intern after an x ray examination had shown a decayed and infected wisdom tooth on the left side of the upper jaw. A fracture of the alveolar process resulted. The patient returned to the clinic six days later and was found to be suffering from a post-operative abscess in the region where the tooth had been extracted, necessitating hospitalization for nine days. No permanent injuries resulted.

The patient brought an action against the society for personal injuries, due to its alleged negligence. The Connecticut Supreme Court of Errors, Haliburton vs. the General Hospital Society of Connecticut, 48 A. 2d 261, set aside a verdict and judgment for the plaintiff for the following reasons: The hospital is a public institution, employing various licensed dentists in a supervisory capacity. The substitute intern had attended Tufts College for three and two-thirds years, but was not licensed to practice dentistry in Connecticut, had not graduated from a dental college, and there was no evidence that he was registered as such a graduate to practice in a clinic in accordance with the Connecticut statutes. The jury's finding was that the employment of the substitute intern constituted corporate negligence.

Under Connecticut law, hospitals are exempt from the general rule that an employer is liable for the acts of an employee performed in the course of his employment, when the hospitals have used due care in the selection of their employees; but, when they fail to use such due care, this exemption is no longer effective and their liability is determined according to the ordinary relationship of master and servant.

An essential element of the liability in such cases is the negligence of the employee. If the employee has not been negligent the employer is not liable. The principles governing malpractice determined the substitute intern's negligence here. The layman's difficulty in comprehending the effect of medical treatment is the same whether the practitioner is licensed or unlicensed. The rule, in Connecticut and elsewhere, is that "no recovery may ordinarily be had in such cases, unless expert testimony supporting the plaintiff's allegation of negligence somewhere appears."

It was held that there was no such testimony in this case. On the contrary, all the medical testimony was to the effect that the operation of the clinic in general, and the treatment by the intern in particular, were either in accordance with general practice, or better. The fact that the operation was followed by an infection raised no presumption of want of proper care or skill.

The plaintiff was not entitled to rely on the principle of *res ipsa loquitur*. To make it apply, the situation or condition "must be such, that in the ordinary instance no injury would result, unless from a careless construction, inspection or user". It could not be said here that, upon the evidence, this condition existed.

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Richard Pearson Strong Medal

Dr. Neil Hamilton Fairley, professor of tropical medicine, London School of Hygiene and Tropical Medicine, was recently awarded the Richard Pearson Strong Medal as "a soldier who has conquered disease, relieved the suffering and saved the lives of innumerable persons in many lands", at a special dinner meeting of the American Foundation for Tropical Medicine at the University Club, New York. During the war, Dr. Fairley was chairman of the combined Advisory Committee on Tropical Medicine to General MacArthur.

The presentation was made by Colonel Strong, United States Medical Corps (retired), for whom the medal and award was named, and who received it first in February 1944. The award, together with a $500 cash honorarium was established by the foundation through a gift by the Winthrop Chemical Company, Inc. It is struck in white metal palladium, which is rarer than gold.

The citation for the 1947 award declared that Dr. Fairley, as Brigadier of the Australian Army Medical Corps, who directed the land headquarters medical research unit of the Australian Army at Cairns, Australia, obtained information on tropical diseases; notably malaria, scrub typhus, and dengue fever which "made possible an earlier termination of the war against the Japanese Empire."

"The medical research unit of the Australian Army", the citation stated, "demonstrated the completely successful chemotherapeutic control of malaria in troops in the South West Pacific. The information obtained, proved an important factor in the success of the widespread campaign of the armed forces of the United Nations by eliminating the greatest medical hazard facing them."

Accepting the award, Dr. Fairley said he did so "on behalf of the one thousand soldier volunteers and the fifty research men, internists, pathologists, entymologists and parasitologists" who worked with him at Cairns, from 1943 through May 1946.

"The human volunteers, infected with diseases for experimental purposes, made a major contribution to the solution of tropical disease problems in the South West Pacific", Dr. Fairley declared. "Without this voluntary assistance and cooperation, rapid answers to essential questions in the control and transmission of malaria, scrub typhus and dengue fever could not have been given to the high command."

Dr. Fairley declared that America and Britain lead the world in advances in malaria control. He named the new British drug paludrine, now undergoing extensive experimentation in the field; and the American development of atabrine and the new drug chloroquine, which is being introduced now for civilian use as aralen, as the latest additions to the medical armamentarium against the disease. "With these drugs and the use of DDT, the conquest of malaria in the tropics has been brought appreciably nearer", Dr. Fairley concluded.

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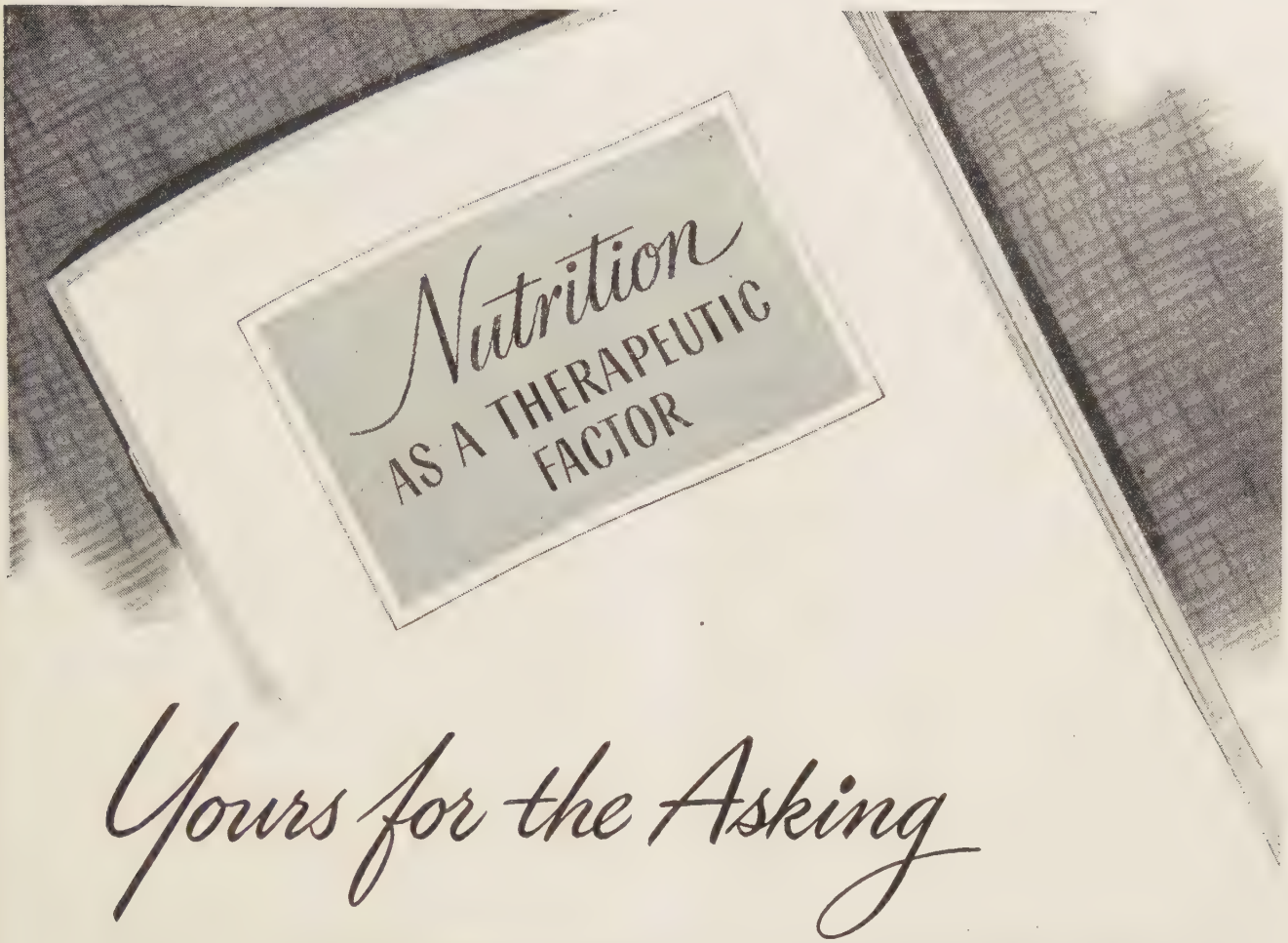

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Tropical Disease Research

Progress in a fight being waged by American and Egyptian doctors working together to conquer the dread tropical disease, schistosomiasis, was the subject of a recent conference at the laboratories of the Sterling-Winthrop Research Institute.

Dr. M. Abdel Azim, director of the bilharzia destruction section of the Egyptian Department of Health, conferred with Dr. Maurice L. Tainter, director of the institute, and Dr. C. M. Suter, who in 1944 had been with him in Egypt studying progress in the battle against the infection. "A large part of the population of Egypt," Dr. Azim declared, "has been freed from the infection."

It is interesting to note that the drug Fuadin, named after King Fuad of Egypt, was originally developed as the result of studies under the auspices of the Egyptian Ministry of Health. Fuadin or Repodral as it is now called, is manufactured by the Winthrop Chemical Company and Winthrop Products, Inc., and is being exported to Egypt where entire villages at one time are being treated with the drug.

Along with the treatment of the people, goes the destruction of the snails living in the Egyptian irrigation ditches, which form the reservoir for the bilharzia infection that causes schistosomiasis. These snails excrete the parasites for about two hours each day, and natives working barefoot in the ditches are attacked by the parasites which penetrate the skin and lodge in the body to cause the protracted chronic disease.

Meanwhile, the institute is continuing studies on the synthesis of new drugs for schistosomiasis. These studies were stimulated by Dr. Azim when Dr. Tainter and Dr. C. M. Suter of the institute's staff visited him two years ago in Cairo.

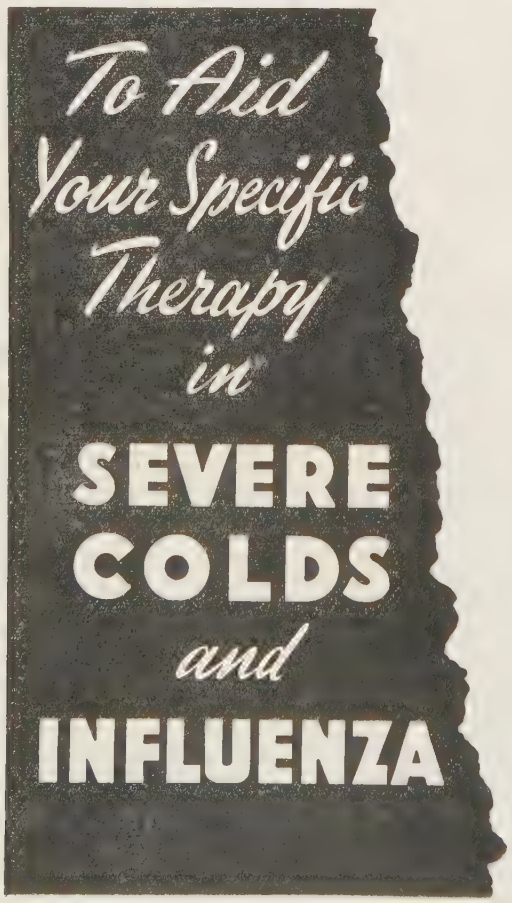
While in this country, Dr. Azim will also visit the National Institute of Health in Bethesda, Md., the University of Minnesota and other centers for tropical disease research.

Outfit for Tuberculosis Specimens

According to *Health News*, December 23, 1946, a change has been made in the outfit distributed by the Division of Laboratories and Research for the submission of specimens to be examined for evidence of tuberculosis. Experience has shown that an ounce or more of sputum, collected over two or three days if necessary, should be available for examination. The outfit is, therefore, considerably larger than the one formerly in use, and requires eleven or twelve cents postage, depending on whether it is mailed from the second or third zone.

The new outfit will be made available in the district laboratory supply stations as rapidly as possible. It will bear the address of the Albany laboratory, where the examinations for evidence of tuberculosis are performed.

Physicians are advised to continue the use of local approved laboratory facilities, when available.



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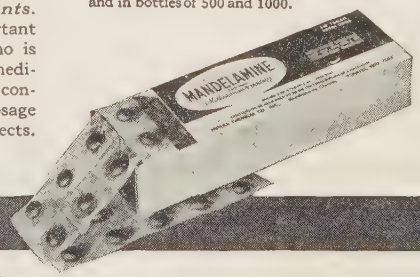

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Rehabilitation Center for Army Hard of Hearing

Brigadier General George C. Beach, Jr., Commanding General of the Army Medical Center and Walter Reed General Hospital, has announced that the army's new rehabilitation center for the deafened and hard of hearing has received eighty-five patients at the Forest Glen Section since it opened in October. Designed as a special unit where the hearing-handicapped can have their disability appraised and corrected to the maximum extent through hearing aids, lip reading and speech correction, the Aural Rehabilitation Center will have sufficient space, equipment and staff to care for as many as two hundred and fifty "students." The GI enrollees—officers and enlisted personnel, women as well as men—will, indeed, be students rather than patients. For persons ordered to the special Forest Glen facility, which is a section of Walter Reed General Hospital, will be those who are finished with treatment and surgery and who now require rehabilitative attention.

Major Henry Cogswell Barnaby, director of the center, is an ear specialist who practiced in Glen Cove, Long Island, N. Y., before the war. Under him there will be a staff of approximately fifty, including twelve instructors in speech reading, six acoustic technicians expert in testing and fitting hearing aids, six technicians who will teach how the device is most efficiently used, five speech correctionists and smaller numbers of specialists in other fields.

Major Barnaby estimates that no

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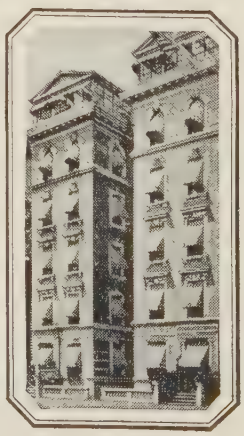
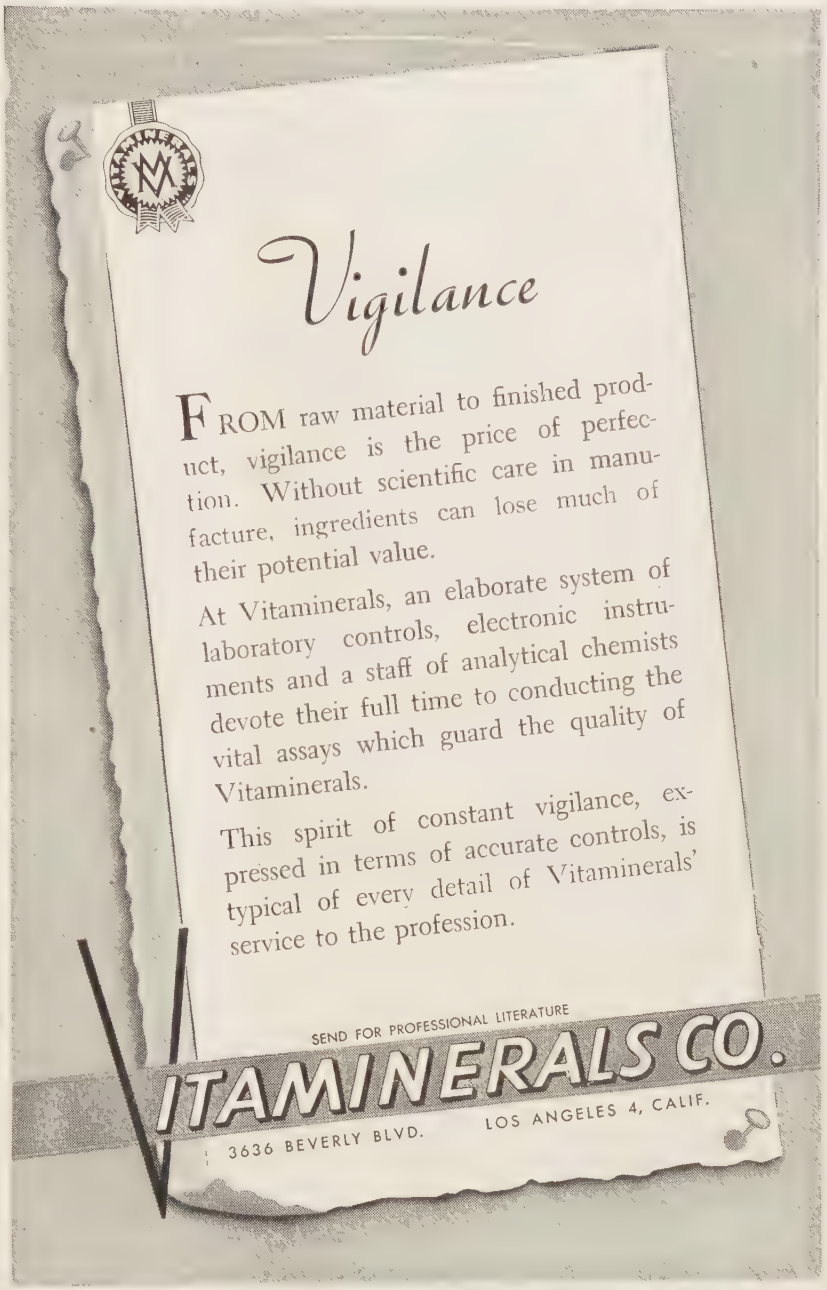


more than twenty percent of the army's deafness and hard of hearing cases can be attributed to trauma; that is, to blast injury or some other combat-connected cause. The remainder were due to disease, infection after-effects or other unspectacular reasons.

Planned as an eight-week program, the rehabilitation course at Forest Glen has as its objective the transformation of every student into an independent, adjusted individual capable of resuming his or her place in society with the least possible handicap economically or socially.

Childhood Diseases Conquered

According to the *Statistical Bulletin*, October 1946, of the Metropolitan Life Insurance Company, phenomenal progress has been made in the control of the four communicable diseases of childhood—measles, scarlet fever, whooping cough and diphtheria. Among Metropolitan industrial policyholders, ages one to fourteen, the age-adjusted death rate from this group of diseases fell from 144.6 per one hundred thousand in 1911-1915, to one twentieth of this (7.2) in 1941-1945, a drop of 95 percent in little more than a generation. In the recent five year period, the mortality from the four diseases *together* was only one tenth that from diphtheria *alone* in the earlier years The largest decline in the death rate, 96 percent, was recorded for diphtheria and for scarlet fever; the decline for measles was 93 percent and for whooping cough 91 percent.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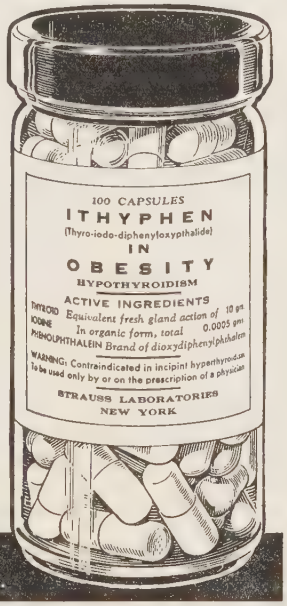

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University of Chicago Cancer Program

Mr. E. C. Colwell, president of the University of Chicago, has announced the broad expansion of the University of Chicago's already extensive work on the cause and cure of cancer into a program that will be one of the largest in the world. His statement followed the filing of an application in Springfield, Ill., for a charter of the University of Chicago Cancer Research Foundation, a non-profit corporation.

Centering around the new Nathan Goldblatt Memorial Hospital, for which the Goldblatt Brothers Foundation recently gave $1,000,000, the cancer program contemplates a capital fund of $4,000,000 and annual support of approximately $600,000. The foundation has been organized as the agency to obtain support for this effort.

Some of the support which the foundation's efforts will provide will be devoted to the Institute of Nuclear Studies and the Institute of Radiobiology and Biophysics, outgrowths of the university's key rôle in the development of the atomic bomb. Two new, powerful instruments, a one hundred million electron-volt betatron, and a ninety-two inch cyclotron, which offer promise of important advances in radiation therapy of cancer, are to be included in the equipment of these institutes. Much of the study of cancer treatment with the increased supply of radioactive materials provided by the atomic piles, will also be carried out through the Institute of Radiobiology and Biophysics.

Some thirty individual research projects, ranging from basic studies such as cell division, to clinical work in surgery and medicine, are now under way at the university and involve fifteen departments in the natural sciences and clinical areas. Of the $600,000 annual budget, $500,000 will be devoted to the expansion of existing research.

Recent important contributions of the university's cancer research program include the demonstration of the rôle of the endocrine glands in cancer, from which developed both the surgical and hormonal treatment of certain forms of the malignancy. Use of estrogens, a female sex hormone, represented the first discovery of a natural product of the body which acts directly upon cancer. The implications of the relation of the endocrine glands to the disease, has stimulated widespread research by investigators on related problems in which gland activity may be involved, such as cancer of the breast.

The first clinical work on the use of mustard gas, which has been found to produce a definite effect upon cancer of the blood producing tissues generally, as compared to the localized effects of radiation, was likewise done at the university. This approach opens up a hopeful method of treating leukemia and allied diseases. Less spectacular surgical techniques, which have been valuable in the treatment of patients, also have been devised at the university. Among these, is the demonstration that extensive surgery is possible in advanced cases of cancer.

Use of Isotopes

Dr. Andrew H. Dowdy, professor of radiology and director of the Manhattan Department, University of Rochester, N.Y., recently asserted before a conference of the American Public Health Association, that the safe peacetime production and utilization of nuclear energy will require the utmost cooperation by industry and science. A relaxation of protective measures, besides endangering the lives of workers, would delay important production and its subsequent benefits to mankind.

Envisioning a situation "almost comparable to a Utopia, Dr. Dowdy explained that the near future of various large-scale projects, from stationary power plants to mobile plants for the propulsion of battleships and submarines, "would seem to be hopeful."

The Manhattan District instituted the national distribution of more than fifty radioactive isotopes, he said. Limiting distribution of the isotopes may be a lack of instruments and well-trained personnel. Their most important and immediate value is as an "investigating tool. Many secrets remain to be pried from the isolated cell and the organism as a whole, relative to their metabolism and physiology under normal and pathological states." He concluded that "the program for the distribution of radioactive isotopes is well under way and from this single feature alone will come many new scientific facts which will be of inestimable benefit to all."

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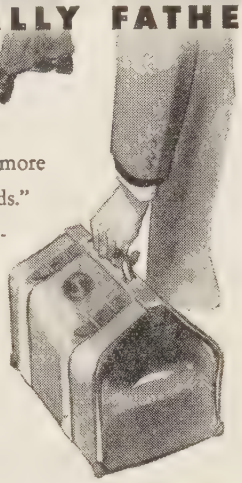

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Aminoprod

A new fortified protein hydrolysate preparation, aminoprod, has recently been announced by The Drug Products Co. Inc., Passaic, N. J.

According to the manufacturers, aminoprod supplies all the essential, as well as certain of the nonessential amino acids, and has a protein content of 67 percent. It contains 90 percent yeast (protein) hydrolysate, together with vitamins A, D, C, B_1, B_2, niacinamide and minerals; iron calcium and phosphorus. Aminoprod is said to be a highly palatable preparation, equally suitable for use in all protein-deficient states, and as a dietary supplement. It is supplied in 8 ounce and 1 pound bottles.

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Hospital Survey and Construction Act

The Hospital Survey and Construction Act, authorizing a nationwide program of hospital construction, requires that standards of construction and equipment be established by the surgeon general, U. S. Public Health Service. These standards will apply to all projects to be built with federal assistance under this legislation. Such standards have recently been drafted by the office of technical services, division of hospital facilities, U. S. Public Health Service, of which Marshall Shaffer is the chief. The committee on hospitalization and public health of the American Institute of Architects approved the standards and submitted them to a special technical committee on architectural standards, which was appointed by the federal hospital council.

After review and approval by this committee, the standards were accepted by the federal hospital council, and they will be incorporated in the rules and regulations of the hospital facilities division. The surgeon general and the federal security administrator will have to approve the rules and regulations before they are published and made available to all persons interested in this program. The standards established constitute the minimum requirements considered necessary to insure properly planned and well constructed hospitals and health centers, but since they are minimum requirements, it is pointed out that they should form a basis only for the development of higher standards.

There has been no attempt, in establishing these standards, to make them coincide with all of the various state local codes and regulations. However, strict compliance with all applicable state and local regulations is required; likewise, compliance is required with minimum standards of construction and equipment promulgated by the state agency administering this program, where such standards are higher than those established by the surgeon general.

Streptomycin Quotas Lifted

In accordance with telegraphic instructions received from Washington, D.C., the Winthrop Chemical Company, Inc., one of the first distributors of the new antibiotic, streptomycin, recently announced that this drug is now available to all hospitals and sanitariums.

Formerly supplied only under allocation by the Civilian Production Administration to selected depot hospitals and other government agencies, although still under government control, streptomycin may now be ordered directly from Winthrop by all hospitals without restrictions.

As was the case with penicillin, due to limited production in the early days, streptomycin may not yet be made generally available through normal drug trade channels, but this action will probably follow as soon as supplies are plentiful.

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Folic Acid in the Treatment of Pernicious Anemia

According to *Health News,* December 2, 1946, Dr. Carl V. Moore, professor of medicine, Washington University, one of the numerous authorities from this country and abroad, brought before the American Dietetic Association some of the newer trends in diet therapy and education. He stated that the use of folic acid in the treatment of pernicious anemia is still in the experimental stage.

Speaking at the recent twenty-ninth annual meeting of the association in Cincinnati, Ohio, Dr. Moore indicated that observations on the response of anemic patients to treatment with folic acid showed that there was still much to be learned about its use, and that the greatest therapeutic value of this substance at present was in the treatment of other macrocytic anemias, including those of pregnancy.

Reporting progress in the analysis of the folic acid content of foods, Oscar Olson, University of Wisconsin, said that fresh, green leafy vegetables, and liver are the best sources of this nutrient. Loss occurs in cooking and when foods are stored without refrigeration.

Dr. Josef Warkany, University of Cincinnati, spoke on "Congenital malformations induced by maternal nutritional deficiency." He emphasized that his observations were based entirely on animal experiments and should not be interpreted as proof that congenital deformities in human beings were the result of malnutrition. His work does indicate, however, that the structure of the animal embryo may be affected by nutritional environment. He is able to produce specific abnormalities of structure in some of the offspring of a litter, by feeding the mother diets deficient in vitamin A or riboflavin. His investigations are being continued.

Emulgen

A new advance in penicillin therapy has recently been announced by the Lakeside Laboratories, Milwaukee, Wis. Penicillin is rapidly destroyed and excreted after injection, and as a result, it has been necessary in many cases to give as high as twelve injections a day. According to the manufacturers, the new product cuts down the necessary injections to three, or less a day. Emulgen is an injection-vehicle consisting principally of sesame oil and cholesterin which easily emulsifies with aqueous solutions of penicillin and slows the absorption of the drug after injection.

When Emulgen and a penicillin solution are mixed and briefly agitated in the syringe, aqueous droplets containing penicillin are coated with lipoidal films. The resulting creamy emulsion flows easily from the syringe and disappears completely from the tissue site into which it is injected, a few hours after it releases the last of its droplets of penicillin into the circulation.

The new Emulgen is said to supercede older emulsifying vehicles and affords a new era of comfort, economy and efficiency in penicillin therapy.

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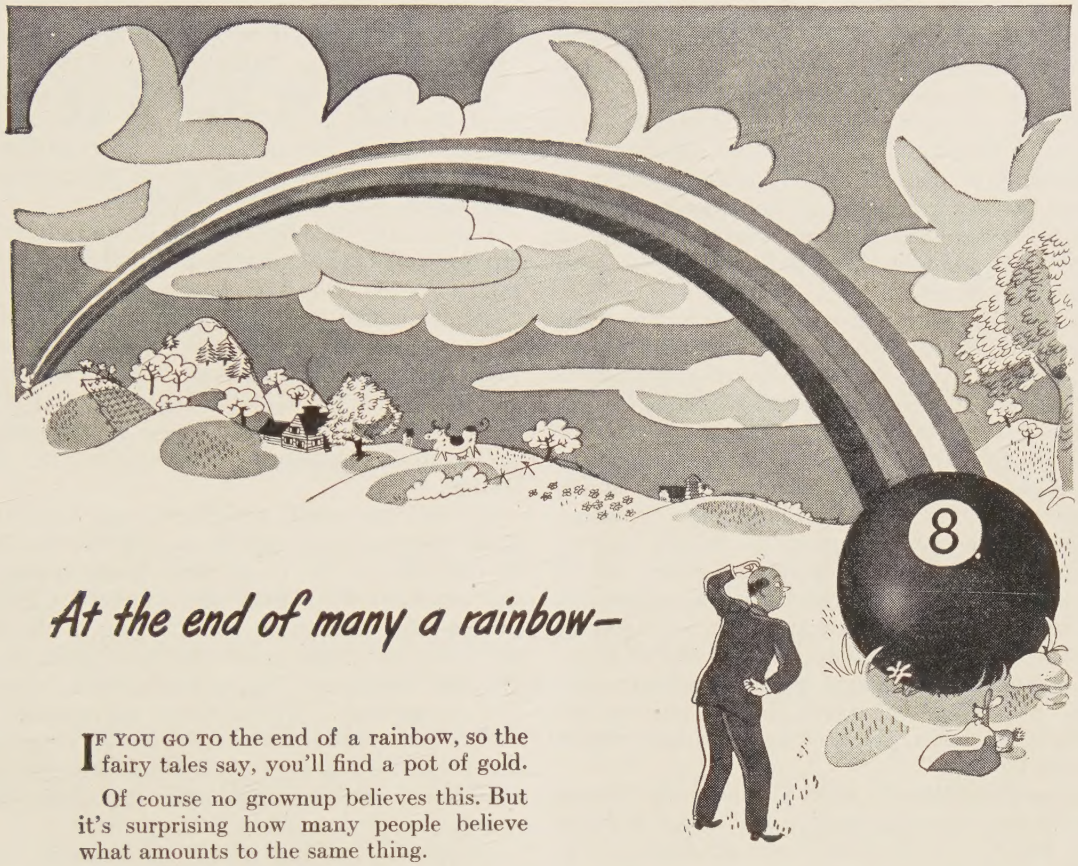

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Infectious Hepatitis from Plasma

Up to the present time, no reports have been received of homologous serum jaundice or infectious hepatitis resulting from the administration of lyophilized plasma distributed by the State Department of Health. However, the following excerpts from a directive published in the *Bulletin* of the United States Army Medical Department (1946: 6, 99-101), dealing with this subject, are important.

"Although the incidence of hepatitis following the administration of plasma is well under 2 percent, a very high incidence may be expected in any group of persons who have received plasma, serum or whole blood containing the infective agent of homologous serum hepatitis.

"The facts presented, in no way detract from the usefulness of plasma when its therapeutic use is clearly indicated. It is, however, strongly urged that the advantages expected to ensue from the use of plasma, be carefully weighed against the possible dangers of the transmission of serum hepatitis. When whole blood, human serum, albumin, amino acids or crystalloids given intravenously, or amino acids and whole protein given by mouth can be used satisfactorily in place of plasma, they should be given preference. The use of human plasma or human serum as control injections, or a diluent or vehicle for other subcutaneous, intravenous or intramuscular medication cannot be too strongly condemned. In view of the availability of immune serum globulin, pooled convalescent human serum should not be used."

Infectious jaundice is now a reportable disease and physicians reporting such cases should indicate whether plasma transfusions were administered to the patients during the previous six months. It would be very helpful if physicians who have taken care of patients with jaundice, prior to the time this disease became reportable, would notify the district state health officer of those cases which have received plasma earlier.

Eye Restoration Clinics

Dr. Paul R. Hawley, chief of the Veterans Administration's medical service, recently stated that veterans administration artificial eye and restoration clinics are in operation in eight cities over the country and soon will be in operation in six others.

At these clinics, eligible veterans either may be fitted with new plastic eyes, or have repairs and alterations made on those they are wearing. Later, the services of the clinics will be expanded to include the fitting and repairing of plastic noses, ears and hands.

Clinics are in operation in Boston, Mass.; New York, N. Y.; Atlanta, Ga.; Cleveland, Ohio; Chicago (Hines), Ill.; Los Angeles and San Francisco, Calif., and Baltimore, Md. Similar clinics will open at a later date in Memphis, Tenn.; Dallas, Tex.; Minneapolis, Minn.; Denver, Colo.; Portland, Ore., and at the army's Valley Forge Hospital, Phoenixville, Pa., when this installation is relinquished by the army and transferred to the Veterans Administration.

In order to supply the clinics with the latest protheses of this type, extensive experiments are being carried out at the University of Maryland, under the supervision of Professor Carl D. Clark. One of the most promising experiments is the development of a seamless plastic glove, designed to fit over artificial hands and to give the hands a natural, lifelike appearance. While these gloves are not yet ready for distribution, experimental progress indicates that they will be available within the next six months to veterans who have lost their hands or arms.

A special training school, to acquaint Veterans Administration doctors and technicians with the progress being made in the experiments and to train them in the art of building the protheses, is being conducted at the University of Maryland School of Medicine. Specialists from the entire country are attending the school.

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